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CONGENITAL CRANIAL OSTEOPOROSIS: ITS ETIOLOGY AND SIGNIFICANCE

A STUDY OF EIGHT HUNDRED NEWBORN INFANTS

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The present study, clinical and statistical, was undertaken with the hope of throwing more light on the etiology and significance of congenital cranial softening, known variously as congenital craniotabes, craniomalacia, "vertex softening" and osteoporosis.[1]

The significance of this condition, a question much debated in pediatric literature, has been the object of numerous investigations undertaken in an attempt to determine its relation to rickets and to the later, or postnatal, craniotabes.

Much less work, however, has been done in the field of the etiology of congenital cranial softening, and although considerable light has already been thrown on the subject, it is still in a state of vast confusion and controversy, which justifies the present study.

Of what interest and value may an investigation of this kind be? First, congenital cranial softening is a common clinical finding, occurring in from 10 to 35 per cent of all newborn infants; secondly, it is a sign readily detected by a mere gentle palpation of the infant's head, a procedure not requiring any special skill on the part of the examiner or the aid of the laboratory and not causing any apparent discomfort to the infant. Therefore, the practical clinical value which such an easily demonstrable clinical finding might possess were it possible to determine definitely its nature and cause is self evident.

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1. Although we preferred to adhere throughout this paper to the term "congenital cranial softening," its synonyms have been used interchangeably whenever reference to works of other investigators has been made.

HISTORICAL REVIEW

Since von Elsässer first published his observations on craniotabes, in 1843, the soft areas in the skulls of infants have become the object of numerous investigations as well as considerable controversy. Von Ellsässer's first observations, however, referred to the later form of craniotabes, or the "true craniotabes," rather than to the congenital form, his youngest patient having been observed at the age of 3½ months.

It was not until 1850 that Bednar observed the frequent occurrence of the congenital cranial defects; he looked on them as an expression of incomplete ossification.

In 1860 Friedleben, on the basis of clinical and anatomic studies, likewise came to the conclusion that these congenital cranial defects are the result of an incomplete ossification which results from nonuniform growth of the bony tissue of the skull.

Broca, in 1862, stated that the most frequent location of congenital cranial softening is the region of the so-called sagittal point, or foramen, which sometimes replaces the two parietal foramens, a point which also forms the center of the obelion. Hughes, however, in 1921, pointed out that the softness found in this location is an expression of osseous immaturity and should be differentiated from the congenital areas of softening found elsewhere in the parietal bone, which are areas of true atrophy or porosis.

Bohn in 1884, as well as Rehn, in 1883, in a follow-up of infants with cranial softening, arrived at a dual conception of craniotabes. These investigators distinguished two forms: the congenital, nonrachitic form, which disappears in the course of the first two months of life, and the rachitic form which develops at the end of the first trimester.

Kassowitz, in the period from 1881 to 1885, arrived at a unitarian conception of craniotabes and concluded, on the basis of clinical and histologic studies, that all forms of cranial softening are rachitic. It was Kassowitz who introduced the term "congenital craniotabes," a term much deplored by Wieland and his school, who stated the belief that congenital cranial softening is etiologically and histologically entirely different from the later form, or "true craniotabes," which is rachitic, and should therefore not be confused with it. Kassowitz also noted the association of congenital cranial softening with other signs of deficient ossification in the newborn, such as large fontaneles, separated sutures and enlarged costochondral junctions. The observations of Kassowitz that there are seasonal variations in the frequency of these skeletal changes in the newborn and that they occur with greater frequency in an urban population than in a rural one led him to believe in the rachitic nature of these changes, a belief which dominated pediatrics for several decades.

Spietschka, in 1886, arrived at the same conclusion as Kassowitz in regard to the nature and etiology of this anomaly and observed that such skeletal changes in newborn infants disappeared on the administration of phosphorus, whereas in infants untreated the process advanced and only 7 per cent of them failed to have rickets later.

Although Pommer as early as 1885 pointed out by microscopic examinations the osteoporotic nature of the congenital cranial defects, it was not until Wieland presented the results of his extensive histologic investigations in 1910 that this view was accepted by most of the modern authorities on the subject. It was Wieland who introduced the term "vertex softening" to distinguish the congenital soft places in the cranial bones of newborn infants, which show a predilection for the parietal bones and lie generally along the course of the sagittal suture, from the acquired form, or so-called "true craniotabes," which is found most frequently in the region of the occiput on both sides of the lambdoid suture.

Wieland's results and conclusions were as follows:

1. The congenital soft places and gaps in the cranial bones of newborn infants are nothing but ossification defects which are due to a temporary discoordination between the rapid growth of the brain and the ossification processes in the vertex of the skull, occurring during the last few months of gestation.

2. This congenital vertex softening occurs in about 10 to 20 per cent of all newborn infants, full term as well as premature, but never in fetuses in the first half of gestation.

3. Microscopically, the locations of the congenital cranial softening, called by Wieland "ossification defects," appear as areas of thin, soft, poorly calcified, punched-out bone which form characteristic gaps in continuity on the inner aspect of the skull, constituting the so-called "resorption defects." These are the result of an increased inner pressure, the pressure of the rapidly growing brain against the limiting brain pan.

4. Histologically, in these osteoporotic areas the osteoid border does not exceed the physiologic limits. In other words, a measurable increase of the osteoid tissue, the sole characteristic histologic stigma of rickets, is not found here.

5. Therefore, these congenital osteoporotic areas can be differentiated readily from acquired craniotabes clinically by their location and time of appearance and histologically by the presence in the latter of an excessive amount of osteoid tissue, such as is associated with lesions of rickets.

6. Congenital cranial softening usually disappears spontaneously in the first few weeks of life. The initial healing may be followed later

by softening, or the initial defect may form the nucleus of an increasing soft area. This later softening, which is synonymous with the acquired or true craniotabes, though more severe and extensive when developing in infants with a congenitally soft skull, is not found more frequently in them.

7. Although congenital cranial softening may be observed more frequently in infants below the normal weight, it is encountered also in large, healthy newborn infants with otherwise normal osteogenesis.

8. The interpretation of this condition as rachitic is derived from confounding the "physiologic osteoid" of the newborn with morbidly increased rachitic osteoid tissue. In short, there is morphologically no anomaly of osteogenesis in this type of osteoporosis, and congenital craniotabes has no relation whatsoever to rickets.

Marfan, in 1921, also basing his assumptions on histologic criteria, arrived at the same conclusion as Kassowitz, who differed from Wieland in not acknowledging the existence of a "physiological osteoid," and expressed the belief that all forms of craniotabes are rachitic in nature. However, Marfan also gave as his opinion that syphilis is the chief cause of rickets and that therefore congenital as well as acquired craniotabes is a manifestation of syphilis. De Stefano (1921), Parrot and Fournier, the famous French syphilologists, shared this opinion with Marfan.

Schloss (*b*), in 1916, though of the same opinion as Wieland in regard to the nature and pathology of the congenital cranial softening, likewise pointed out the difficulties in the histologic interpretation of cranial lesions and the lack of a uniform criterion of what constitutes rickets of the skull.

Hughes, in 1918-1921, advanced the theory of the mechanical causation of congenital as well as of acquired craniotabes. He asserted that the craniotabes arising during the first few months of infancy is in many, and probably in most, cases only a fresh manifestation of the congenital form. The observed differences in position of the soft areas in the congenital and in the acquired form are, according to him, exactly what would be expected if the two conditions were identical, for in both forms the areas occupy the most dependent portions of the skull. In fetal life cranial softening is brought about by a double form of pressure, that of the lower uterine segment and pelvic bones against the outer strata of the skull and that of the growing brain against the inner strata. As proof of the mechanical causation he pointed out, first, that congenital craniotabes occurs only in infants born by vertex presentation and, second, that in all of his 51 infants with congenital craniotabes the softness disappeared rapidly in those places which were situated outside the new regions of increased pressure after birth. Histopathologically both lesions are true atrophies, of variable degree, of the preformed

bone. Hughes concluded that although the mechanical causation is the only certain element in the causation of craniotabes in general, there must be also an organic cause acting as a decalcifying factor. He reasoned that, while the great majority of infants are subjected to closely similar mechanical conditions, in only a minority does cranial softening of any appreciable degree develop. He suggested as a possible etiologic factor a maternal antepartum dietary deficiency, and although the association of both forms of craniotabes in his series of infants with rickets and syphilis was not convincing, he stated the belief that their more remote causality as a morbid, decalcifying factor could not be excluded. Hughes said he was in favor of allying the congenital as well as the acquired craniotabes with rachitic phenomena in general, because of a seasonal variation in the frequency of these conditions which was observed by him in his series. This seasonal variation will be referred to again later in this paper.

Schwarz, in 1920, in studying the incidence of craniotabes in infants during the first year of life, observed that in his series it was greatest among Negro infants, in whom the condition occurred in 39.2 per cent, as compared with a maximum of 19 per cent and a minimum of 11.5 per cent in infants of other races. In this investigation, however, no differentiation was made between the acquired and the congenital form of craniotabes. Since some of the infants were examined for the first time a few weeks after birth, it would appear that in some cases the congenital form also must undoubtedly have been present.

Wilson and Kramer, in 1923, and Barenberg and Bloomberg, in 1924, first introduced determination of the blood chemistry into the study of craniotabes in general. They found no significant alterations in the blood calcium and phosphorus of infants with craniotabes under 4 months of age and concluded that chemically, roentgenologically and clinically these infants failed to show evidences of rickets. Again no differentiation was made in the investigations between the congenital and the acquired form of craniotabes, and it appears probable that in some cases the congenital form may have been present in that series too.

Rosenstern, in 1922, as well as Hottinger (*a*), in 1922 to 1928, observed that congenital cranial softening occurs less frequently in the premature infant. While Rosenstern observed it in 7 per cent of his series of subjects, Hottinger found it in 11 per cent of his series of 188 infants. On the basis of these observations Rosenstern concluded that congenital osteoporosis is less frequent in the premature infant because the development of the brain, which is definitely a contributing factor in the causation of congenital osteoporosis of the cranium, is greatest during the last month or two of gestation.

Comby, in 1927, concurred with Wieland's observations that congenital cranial softening is found in strong as well as in debilitated

infants and that the area consolidates spontaneously without any treatment. He concluded, as a result of his investigation, that, while late craniotabes may be due to rickets, the congenital form is simply a retardation in ossification, a "physiological craniotabes," and does not have any connection with this disease.

Abels and Karplus, in 1927, published their observations on several thousand newborn infants. These authors observed that rickets occurred in 80 per cent of infants who at birth presented some cranial softening, as compared with 12 per cent of those whose skulls at birth were hard. They therefore termed the anomaly "prerachitic osteoporosis" and expressed the belief that it constitutes the long-sought-for uniform morphologic basis of rachitic disposition. They also maintained that congenital cranial softening occurs more frequently in children of primiparas than in those of multiparas, that it is found only in infants born by vertex presentation, and that it occurs mostly in infants of weight and length below the average, with other signs of delayed ossification, such as wide sutures and fontanels with soft edges. They also observed that this congenital cranial softening disappears soon after the cessation of active intrauterine pressure and that there is a seasonal variation in its incidence, with winter as the most favorable season for its occurrence. These authors concluded that congenital osteoporosis should be considered not as physiologic but as prerachitic and as being caused by exogenous mechanical forces, such as contacts with the maternal pelvis, operating with a certain constitutional inferiority and possibly with a maternal dietary deficiency as a contributing factor.

Arluk, in 1928, likewise observed the greater frequency with which congenital cranial softening occurs in infants born of primiparas, as well as the greater predisposition of these infants to rickets. He also noted that there is a seasonal variation in the incidence of congenital osteoporosis, with winter and spring as the seasons of its maximum frequency. This author, however, failed to confirm the observations of Abels and Wieland as to the greater frequency of this condition in infants below the average weight. Furthermore, Arluk's observation that premature delivery increases the frequency of congenital craniotabes in the newborn is not in accord with that of Rosenstern and of Hottinger, who found it to be a relatively rare condition in the premature infant.

Hess, in 1929, in his book "Rickets, Osteomalacia and Tetany," made the statement that "the significance of osteoporosis and its relation to rickets is unknown, but the fact that true craniotabes shows a tendency to develop at the site of the congenital cranial defect must be regarded as evidence in favor of osteoporosis predisposing to rickets."

Toverud, in 1932, on the basis of a study of 200 newborn infants, concluded that a maternal deficiency in mineral—i. e., calcium and

phosphorus—during pregnancy is responsible for the occurrence of congenital osteoporosis. She found that almost all the "hard skull" infants in that series were the offspring of mothers who had had an adequate mineral intake during pregnancy. Toverud likewise stated that congenital cranial softening is not an isolated phenomenon but a part of a generally defective calcification or osteoporosis in all the bones of the newborn infant. It was shown experimentally in dogs (Toverud and Toverud) that a mineral deficiency in the mother animal during gestation resulted in a lowering of the calcium and phosphorus of the bones of the newborn young, with development of osteoporosis.

In this connection it is interesting to mention that Korenchevsky, in 1922, showed experimentally that diets deficient only in calcium result in osteoporosis.

In a more recent publication (1934), Toverud reported a study of 100 mature and premature infants, in which a decrease of the ash and of the calcium content of the ash was observed in some of the mature and in all the premature infants born of mothers who during pregnancy had been on a diet poor in calcium and phosphorus. A widening of the osteoid zone in the parietal bones, ribs and mandible was also observed in these infants.

Coons and Blunt, in 1930, noted from roentgen ray examinations of the wrists of normal infants that the calcification of the epiphyses of the radius and ulna was best in infants whose mothers had the highest retention of calcium and phosphorus during pregnancy.

Booher and Hansmann, in 1931-1932, found no difference in degree of calcification of the tibias among newborn infants of mothers whose calcium intake varied within fairly wide limits.

Jundell, in 1931, observed that the administration of cod liver oil or irradiated ergosterol (vigantol) during the last few months of pregnancy in no way lowered the frequency of congenital vertex softening of the skull nor did it prevent the development of postnatal craniotabes in the infant. That author concluded that neither congenital vertex softening nor postnatal supraoccipital softness has any relation to rickets and that craniotabes should be looked on as a physiologic or hypoplastic process.

Maxwell, Hu and Turnbull, in 1932, definitely demonstrated the occurrence of fetal rickets in infants born of Chinese mothers who had suffered from osteomalacia during pregnancy. They pointed out that osteoporosis of the cranial bones is a frequent accompaniment of the disease in such infants.

Eliot, in 1933, in her study of rickets in Puerto Rico, reported the occurrence of marked osteoporosis in 59 children—approximately 10 per cent—who, with the exception of 2, had no rickets. Eliot suggested

that the osteoporosis was due to gross inadequacies in the Puerto Rican diet, especially with respect to calcium.

Bang, in 1937, reported determinations of the calcium and the phosphorus content in the blood of a group of infants suffering from congenital cranial softening. No alteration in either of these elements was found by him. The same observation had been made previously by other investigators (Garrahan and Bettinotti; György [*a*], Hottinger [*b*]).

Finally, Sontag and Harris, in 1938, concluded from roentgenographic examinations of the tarsal bones of normal infants that the circular tarsal striae frequently found in roentgenograms of 1 month old infants not only are the result of disturbances in growth produced by the process of birth itself but are influenced by such factors as the maternal nutrition and health during pregnancy.

To summarize in outline the various concepts of its cause, congenital cranial softening has been regarded variously as due to the following conditions:

1. Rickets (Kassowitz; Marfan; Spietschka)
2. Syphilis (Marfan; de Stefano; others)
3. Mechanical pressure effects
   a. Endogenous (Wieland)
   b. Exogenous (Abels and Karplus)
   c. Mixed (Hughes)
4. Mechanical plus organic factors, i. e., constitutional, dietary or infectious factors (Hughes; Abels)
5. Antepartum dietary deficiency of the mother's diet (Toverud; Abels)
6. A developmental defect in construction (Hess)
7. A physiologic factor (Comby; Jundell; Furst)

In regard to the causation of congenital cranial softening or craniotabes as compared with that of the postnatal or acquired form, the various concepts are as follows:

1. All forms of craniotabes are rachitic (Kassowitz; Spietschka).
2. All forms of craniotabes are syphilitic (Marfan; de Stefano).
3. No craniotabes is rachitic (Comby; Jundell; Miani; Furst).
4. No craniotabes is syphilitic (all except Marfan and his school).
5. Postnatal craniotabes is nothing but a fresh manifestation of the congenital form, both being caused by mechanical pressure effects (Hughes).
6. Congenital craniotabes is nonrachitic, i. e., physiologic (Wieland; Dunham; Eliot [1925]; Schloss [*b*]; Finkelstein) or prerachitic

(Abels), while all acquired craniotabes, or "true craniotabes," is rachitic (Wieland; Abels; Eliot and Park; Dunham; Rosenstern and Bruns).

7. Congenital craniotabes is nonrachitic, while the postnatal or acquired craniotabes is prerachitic, i. e., "rachitis praecox" (György [*a*]).

8. Congenital craniotabes is nonrachitic, while the acquired form may be of one of two types, the rachitic or the physiologic, a simple osteoporotic process (Hess; Hojer; Barenberg and Bloomberg; Wilson and Seldowitz; Sheldon).

CAUSES OF THE CONTROVERSY AND THE PRESENT STATUS OF KNOWLEDGE

One may readily see from the foregoing review that, although a great deal of work has been done in the study of congenital cranial softening, the subject is still far from being clarified and at present there is no uniformity of opinion regarding the genesis of the anomaly.

What are the reasons for so much controversy? The most important are: (1) the lack of uniform histologic criteria for judging the significance of the osteoid tissue of the infant skull and what does or does not constitute rickets of the skull; (2) the lack of a uniform objective criterion in the diagnosis, arising from the difficulty of determining the degree, character and extent of cranial softening—a lack which prohibits comparison of the results obtained by different investigators; (3) the difficulty in clinical differentiation between the congenital and the acquired form of cranial softening, especially if the infant has not been observed constantly since birth, the result being that many series of cases of so-called acquired craniotabes undoubtedly include cases of the congenital form; (4) failure to apply statistical methods of analysis in order to determine whether the results obtained by the investigation are statistically significant, so that in many instances conclusions undoubtedly have been drawn from an insufficient number of cases.

What is the present state of knowledge in regard to the pathogenesis, significance and clinical features of congenital cranial softening?

Clinically, congenital cranial softening can be observed at birth. It shows a definite predilection for the parietal bones, especially for the region of the vertex, and it generally follows the course of the sagittal suture. When the affected bone is gently palpated in situ, it usually feels resilient and snaps back as the finger is released, much like an indented ping pong ball or the crown of a derby hat, while in the more severe forms it is apt to feel like parchment or crackling eggshell or even to be soft and mushy.

Anatomically, or macroscopically, congenital cranial softening or craniotabes appears most commonly in the form of circumscribed, thin

areas of bone, which are punched out or gradually fade into normal bone (Wieland; Hughes).

Chemically, a diminished content of calcium and phosphorus salts has been found at the site of the porotic bone (Hess).

In regard to its histologic features, the majority of investigators agree with Wieland and consider it an established fact that congenital cranial softening or craniotabes is purely an osteoporotic rather than a rachitic or syphilitic manifestation of the skull.

As to its etiology, while most investigators, among them Wieland, Jundell, Comby, Eliot (1933) and others, have said they considered the condition a mere delay in ossification, of no pathologic significance whatever, almost equally as many, among them Hughes, Abels and Karplus, Hess (1931), Toverud and Toverud and others, have asserted that, though in itself not rachitic, it may possibly cause a predisposition to rickets. In recent years it has been looked on by Toverud (1932) as an expression of general skeletal osteoporosis. While Abels and Karplus and Hughes suggested the possibility of an antepartum dietary deficiency of the mother as one of the etiologic factors, Toverud definitely postulated this theory and presented some experimental evidence to support it.

To sum up the present state of knowledge of the congenital cranial softening, its etiology, course and significance are still a matter of controversy.

One may readily see from the foregoing review that, although a great deal of work has been done to determine the clinical significance of congenital cranial softening, much less work has been done in the field of its etiology, especially with respect to correlation of antepartum, climatic and racial factors. This justifies the present study.

Likewise there is at the present time an increasing interest in the study of the infant in his relation to maternal antepartum conditions. The importance of studies which are directed toward clarifying these questions so vital to the health of the mother and child is self evident. By means of the present study we hope to throw more light on a condition commonly found in newborn infants and to see whether it is open to prophylactic measures.

NATURE AND NEW ASPECTS OF THE PRESENT STUDY

In the present study the following factors were considered in their relation to the incidence of congenital cranial softening: (1) the physical status of the infant, with special reference to such aspects as weight, length, head circumference and tissue turgor; (2) all known antepartum factors which might affect the calcification of the infant's skeleton in

general, such as the maternal diet, health and exposure to sunshine; (3) race, and (4) climate, from the standpoint of the effectiveness of the available ultraviolet radiations. Consideration of the fourth factor, climate, also included a study of its relation to the severity of the congenital cranial softening and comparative study of the geographic distribution and the frequency of the anomaly as given by different authors.

The results obtained were analyzed by the use of widely accepted statistical methods, and a comparison of results was made with those obtained by other investigators.

This study differs from those previously reviewed in the following features:

1. Race has been considered as a possible etiologic factor.

2. The alleged relation of congenital cranial softening to rickets has been investigated by determining the frequency of its occurrence under climatic conditions such as exist in southern California, where the incidence of rickets is relatively low.

3. Not only the calcifying factors of the maternal antepartum diet have been taken into consideration as an etiologic factor, but also all other known antepartum factors which might possibly influence the calcium and phosphorus metabolism of the pregnant mother and thereby be reflected in the state of calcification of the infant's cranial bones.

4. An attempt has been made here to evaluate Toverud's theory that a maternal mineral deficiency during pregnancy is the main etiologic factor of congenital cranial osteoporosis.

5. The results have been analyzed by modern statistical methods.

6. Congenital cranial softening in North American infants has been comprehensively studied.

The various phases of this study will be discussed in detail in the subsequent sections.

MATERIAL

The present study was conducted in the obstetric wards of the Los Angeles County General Hospital.

The infants studied consisted of a nonselected group of 800 newborn babies, chosen at random from the general nurseries, where only apparently mature and essentially normal infants, weighing not less than 5½ pounds (2,495 Gm.), are kept.

Three hundred and thirty-two detailed antepartum histories were obtained directly from the mothers by one of us and supplemented by data from hospital records. We tried to include in this series mostly mothers of offspring with either very hard, thick, nonflexible cranial bones or with a marked degree of cranial softening. However, mothers of a number of infants of intermediate groups were likewise included here. All mothers whose blood gave positive Wassermann and Kahn reactions were excluded.

Because of our interest in race as a possible etiologic factor in congenital cranial softening, we divided our series of infants and mothers into three main racial groups. The classification was made from the standpoint of the degree of pigmentation of the skin, the greater susceptibility of the dark-skinned races to rickets and to postnatal craniotabes being kept in mind. The subjects considered racially were thus largely represented by the following three groups: (1) the white, which included mostly those of American-born and foreign-born parents of northern and central European extraction; (2) the Negro, which consisted entirely of native or American-born Negroes, and (3) the Mexican, in which we included the native or American-born, as well as the Mexican-born, olive-skinned Mestizo, who in Mexico and in the western United States is known as a person of mixed Indian and Spanish blood. Since the great majority of Mexicans who are of the lower economic levels in California and are thereby eligible for care at the Los Angeles County General Hospital are, with few exceptions, these olive-skinned Mestizos with predominantly Indian characteristics, we felt that they constitute a well defined racial group and should be classed separately as such.

Of the 800 infants, 61.4 per cent belonged to the white racial category, 31.9 per cent to the Mexican and 6.7 per cent to the Negro.

Of the 330 mothers from whom complete histories were obtained, 200, or 60.6 per cent, belonged to the white racial category, 98, or 29.7 per cent, to the Mexican and 32, or 9.7 per cent, to the Negro.

As to the economic status, the mothers of our series of infants were all ward patients. The group therefore consisted almost entirely of women of the lower economic levels, who either were receiving limited county or private charity aid and therefore warranted free care or had an income at most not above $80 or $100 a month per family of two and were required to pay for hospitalization. In our series the first group constituted by far the majority.

CONDITIONS OF THE PRESENT STUDY

This investigation was conducted for eleven consecutive months, from July 1935 to June 1936. The last 100 infants were examined during the months of June, July and August of 1937. The last seventy histories were obtained during the same period. The study, therefore, extended throughout almost two years and included all four seasons of the year.

In regard to the quantity and quality of the available sunshine in Los Angeles, according to the Annual Meteorological Summary a fifty year average of the records of the United States weather bureau shows that there are only ten days in the year without sunshine; that the yearly average percentage of possible sunshine is 72, with a minimum of 63 and a maximum of 79, and that the total yearly average number of hours of sunshine is 3,214. The minimum seasonal altitude of the sun is below 35 degrees for only one month in the year, that month being December, when the maximum daily altitude of the sun at noon is 33 degrees. The maximum seasonal altitude, which is 79 degrees, occurs in June. This is well above the minimal altitude set by Tisdall and Brown (1929) for antirachitic effectiveness of sunshine.

Table 1 illustrates the above climatologic data. Corresponding data for the period of study are presented for comparison. The table clearly demonstrates that the climatic conditions during the period of study did not differ materially from the usual climatic conditions in this locality.

TABLE 1.—*Meteorologic Summary for Los Angeles (Compiled from the U. S. Weather Bureau Records of Monthly and Annual Meteorologic Summaries of Los Angeles and the American Effemeris and Nautical Almanac, 1938)*

Month	Mean Temperature, F.		Moisture: Relative Humidity, % 12:00 Noon		Moisture: Precipitation, Inches		Average Number of Days: Clear		Partly Cloudy		Cloudy		Without Sun		Sunshine: Total Hours		Sunshine: Per Cent of Possible		Maximum Daily Altitude of Sun § (Average)
	Normal* Average	Study Period Average	Normal†	Study	Normal*	Study	Normal*	Study	Normal*	Study	Normal*	Study	Normal*	Study	Normal‡	Study	Normal‡	Study	
January	55.2	54.7	45	42	3.16	1.80	15	14.7	9	9.0	7	7.3	2	2.0	219	215.2	70	68.3	35.5
February	56.2	57.3	51	49:3	2.94	5.78	12	12.3	9	4.3	7	11.7	1	4.0	212	183.4	68	59.0	43
March	57.9	57.6	48	49.3	2.62	3.23	13	15.7	10	7.7	8	7.7	1	1.7	254	250.7	68	67.3	54
April	60.0	61.2	53	51	1.06	1.46	12	11.7	11	11.3	7	7.0	1	1.3	266	262.8	68	67.0	66
May	62.5	63.0	58	58	0.43	0.10	11	13.7	14	9.3	6	8.0	1	4.0	274	265.3	63	61.7	75
June	66.5	67.7	57	56.3	0.09	0.07	13	17.0	14	11.0	3	2.0	0	0.3	301	318.9	70	73.7	79
July	70.5	72.1	54	51	0.01	0.00	16	21.0	14	7.7	1	2.3	0	0.3	342	338.3	78	77.0	77.5
August	71.3	73.0	54	52.3	0.03	0.04	18	20.0	12	8.3	1	2.3	0	0	328	325.2	79	78.3	70
September	69.5	70.7	52	52.5	0.15	0.02	17	17.0	11	11.5	2	1.5	0	0	284	337.8	77	70.5	59
October	65.5	67.2	48	44	0.64	0.65	17	17.0	10	8.0	4	6.0	1	1.0	266	251.1	76	71.0	47
November	61.7	64.3	38	31	1.19	0.65	18	17.5	8	10.0	4	2.5	1	2.0	244	248.5	78	79.5	37.5
December	56.9	59.0	44	42	2.67	3.53	17	15.0	8	7.0	6	9.0	2	2.0	224	217.1	73	70.5	33
Yearly average	62.8	64.0	50	48	14.99	17.33	179	192.9	130	105.1	56	67.3	10	18.6	3,214	3,214.3	72	71.0	56.4

* Based on a period of fifty-eight years.
† Based on twenty years.
‡ Based on thirty-nine years.
§ Based on values at noon on the fifteenth day of each month.

METHODS OF INVESTIGATION IN EXAMINATION OF INFANTS

A complete, detailed physical examination was made of 700 of the infants. The occipitofrontal circumference of the head, the circumference of the chest and abdomen and the body weight and crown-heel length were the measurements obtained. Both positive and negative findings were recorded. The examination of the last 100 infants was limited to a general clinical inspection, a detailed examination of the skull and a general appraisal of the skeletal and muscular development; the aforementioned measurements were likewise recorded.

Five hundred and twenty-eight of the infants were examined on the second day of life, 246 on the third or the fourth day and 26 on the first. Most of the infants with cranial softening were rechecked shortly before their discharge from the hospital on the ninth day.

The infants were arbitrarily divided into two main groups:

1. The normal, which included all well developed and well nourished infants whom physical examination revealed essentially normal, except for such abnormalities as minute developmental defects and physiologic birth injuries.

2. The so-called abnormal, which included, first, infants with major congenital anomalies; second, those with birth injuries, including cephalhematoma, and third, all infants with obvious signs of immaturity and congenital debility (Parmelee; Grulee and Bonar [1937]). The infants of mothers whose blood gave positive Wassermann reactions were likewise tentatively included in this group.

A special notation of the following findings was made and their association with the presence or absence of cranial softening observed: (1) nature of the skeletal development, as judged by body weight, crown-heel length and occipitofrontal cranial circumference; (2) type of skull, its size and shape; (3) size of the fontanels; (4) separation or approximation of cranial sutures; (5) degree of cranial molding; (6) presence or absence of cranial or facial asymmetry; (7) presence or absence of cephalhematoma; (8) shape of the chest—size of the costochondral junctions; (9) degree of tibial bowing; (10) degree of maturity; (11) presentation and position at birth, and (12) presence or absence of minute developmental defects and other congenital anomalies.

Method of Examination for Cranial Softening.—The following technic was used in the examination of the infant's head for cranial softening:

The head of the infant, facing the examiner, was held between both hands, and the cranial bones were gently and thoroughly palpated with the tips of the index and middle fingers. The softening could usually be perceived by comparatively gentle, very light or moderately light pressure. Stronger pressure was not exerted, the great sensitivity of the periosteum being kept in mind.

All degrees of definite cranial softening were considered as osteoporosis, though a slight localized yielding or compressibility without a rebound of the indented portion of the bone was disregarded. The latter type of localized yielding is frequently observed over a small symmetric area, about 1 by 1 cm. in diameter, in the region of the parietal foramena or the "sagittal foramen" replacing them, which lies about 2 and 2.5 cm. above the posterior fontanel. Only when a more extensive focus of actual softening occurred in that region was it used in the compilation of our morbid series. Care was taken to avoid a common source of error, which is to confound a yielding or rocking of the entire bone—which may occur when pressure is applied along the suture line—with actual softening (Levinson; New Haven study).

We have observed that cranial softening may be of the following three main types, all of which may occur to a greater or lesser degree in the same infant:

1. The "resilient" type, which is the mildest form of softening and requires a moderately gentle pressure to be perceived. In this type there may be one or several fairly sharply circumscribed areas confined exclusively to the parietal bone, usually to the region of the vertex along the course of the sagittal suture and occasionally including also the supratemporal region. The indented portion of the involved bone appears resilient and, as one's finger is released, springs back much like a ping pong ball or the crown of a derby hat.

2. The "parchment" type, which is the more severe and extensive softening, which requires but a very light pressure to be perceived, and in which the affected bone presents a crackling sensation resembling that produced by parchment or eggshell.

3. The most severe softening, in which the affected bone is thin and membranous and presents a soft, flabby sensation—a type exceedingly infrequent in our series of infants and accompanying only an extensive and bilateral involvement of the parietal bones.

We found that the parchment type of softening was usually more extensive than that of the resilient and that while both occurred either unilaterally or bilaterally, in the soft, flabby type a bilateral involvement was always the rule. In all instances the softening was definitely asymmetric, one parietal bone being much more affected than the other. The parietal protuberance was not found by us to be affected even in association with the most extensive forms of softening. In only 3 of our infants were other cranial bones besides the parietal affected. In these, small portions of the temporal and frontal bones adjacent to the parietal were found to be flexible and resilient.

Classification of Infants According to Type of Skull.—The infants were arbitrarily classified according to type of skull into three main groups, the nomenclature for which was taken from Toverud, though the description has been somewhat modified to fit best into the picture found in our particular series of infants: group I, infants with "hard" skulls, including those with no yielding or compressibility of bone on light or moderate, but gentle pressure; group II, those with "soft" skulls, including infants presenting on light pressure a definite yielding or softening of more than one half of the parietal area usually involved, namely, the vertex, and group III, infants with "transitional" skulls, including those with a lesser degree of definite softening, no matter how small the area of involvement. In other words, those with "soft" skulls presented an extensive or a marked degree of softening, while those in the "transitional," or intermediate, group presented the slight and moderate forms.

We fully realize the limitations of such an arbitrary classification, based on purely subjective criteria of diagnosis. We have found, however, that while the infants with "hard" skulls could be readily differentiated from those with "osteoporotic" skulls—namely, the "transitional" and the "soft" skull group combined—it was much more difficult and not always possible to draw a sharp line of demarcation between those with "soft" skulls and some of the "transitional" group. We tried to solve this difficulty by placing the infants thought, but not known, to have "soft" skulls in the intermediate group, those with "transitional" skulls.

Weight.—The weight, which had been obtained in the delivery room at birth, was recorded in pounds and ounces and later transposed into the terms of the

metric system. The infants were divided according to weight into "large," "average" and "small," by the following method:

A sample tabulation of 200 actual weights was done, those of the first 10 infants from each month of study being taken in order to obtain an even distribution. The mean as well as the probable error of the mean was determined, the former being 7.52 pounds (3,402 Gm.) and the latter ± 0.717. By this procedure the middle range, which included 50 per cent of the total number of weights, was obtained. It was found to comprise all weights ranging from 6 pounds 13 ounces (3,090 Gm.) through 8 pounds 3 ounces (3,714 Gm.). Infants with weights within this range constituted the "average" group; 51.6 per cent of our infants were included in that group. Those whose weights fell below the lower and above the upper limit of this range constituted two distinct weight groups, the "small" and the "large," comprising 24.4 and 24 per cent of the total number respectively.

Body Length.—The crown-heel length was carefully obtained at the time of examination and recorded to the nearest centimeter. The infants were divided according to length into "large," "average" and "small," according to exactly the same procedure as for weight. The mean length was found to be 51.71 cm. and the probable error ± 1.39. The "average" length group, which comprised 47.8 per cent of the total number of infants, included those with lengths ranging from 50 through 52 cm.; while the "small," including all those with lengths below 50 cm., and the "large," or all those with lengths above 52 cm., comprised 23.2 per cent and 29 per cent of the infants respectively.

Head Circumference.—The occipitofrontal head circumference was taken with a steel tape at the prominent part of the brow and the occiput at the time of examination and the measurement was recorded to the nearest half-centimeter. The same procedure as that used in the case of weight and length was followed for dividing the infants according to the size of their head circumferences. The mean head circumference was found to be 34.28 cm. and the probable error ± 0.90. The "average" group, which comprised 50.6 per cent of the total number of infants, included those with head circumferences ranging from 33 through 35 cm., while the "small," including all with measurements below 33 cm., and the "large," or all those with measurements above 35 cm., comprised 24.4 per cent and 25 per cent of infants respectively.

Anterior Fontanel.—The anteroposterior and the lateral diameter of the anterior fontanel were measured by one of the following two methods: In the first, a small caliper was used, the blunt, well padded points of which were applied to the corresponding angles at the margins of the fontanel and the distance between them determined to the nearest centimeter by the aid of a small transparent ruler. In the second, a method almost as accurate and not requiring the assistance of another person, the measurements were obtained by the use of the finger tips, the measurements of the finger tips having first been taken (New Haven study).

The statistical procedure previously outlined was followed to divide the infants into "large," "average" and "small," according to the size of the anterior fontanels. Since it was necessary to deal with two measurements to express the size of the fontanel, the product of these measurements was obtained in each case to simplify the tabulation and calculations. The mean was found to be equal to a product of 6.02 cm., and the probable error of the mean was ± 3.70. The "average" group, which included all having fontanels with a product of the corresponding anteroposterior and lateral diameters ranging from 3 through 8 cm.,

comprised 47.3 per cent of the total number of infants. To this group belonged those having fontanels with diameters such as 1.5 by 1.5 cm., 2 by 2 cm. and 2 by 3 cm. To the "small" group, which comprised 26.7 per cent of infants, belonged those having fontanels with a diameter product of below 3 cm. (e. g., 1 by 1 cm. or 1 by 2 cm.), while to the "large," which comprised 25.8 per cent of infants, belonged all those whose fontanels had a diameter product of above 8 cm. (e. g., 3 by 3 cm., 3 by 4 cm., or 4 by 4 cm.).

METHODS OF INVESTIGATION IN EXAMINATION OF MOTHERS

Detailed antepartum histories were obtained directly from the mothers by one of us, who has an adequate knowledge of Spanish and therefore had no difficulty in obtaining satisfactory histories from the Mexican mothers. These were supplemented by data obtained from the hospital records concerning such information as the results of the maternal physical and laboratory examination, the type of delivery and the presentation and position of the infant at birth.

Special consideration was given in taking the antepartum histories to all known factors which might directly or indirectly affect the calcium and phosphorus metabolism during pregnancy—namely, (1) type of diet, with special reference to its calcifying factors, (2) amount of exposure to sunshine, (3) total number of childbirths and the interval between them, (4) health during pregnancy, with special reference to hyperemesis and toxemia of pregnancy, and (5) home environment from the standpoint of the availability of sunshine, including whether the environment was urban or suburban.

The following additional factors were also noted: (6) amount of physical work and rest during pregnancy, (7) economic status and (8) condition of the maternal teeth.

Data obtained from the hospital records on the mothers included (1) Wassermann and Kahn reactions of the blood, (2) findings on physical examination, general as well as obstetric, (3) presence or absence of toxemia of pregnancy and (4) type of delivery.

In regard to the diet, the histories contained a comprehensive list of foods, and the mothers' statements of how frequently and in what amount a given food had been consumed were recorded. The Mexican mothers were, in addition, questioned carefully regarding the intake of the maize, or lime-treated corn, "tortilla" and of "frijoles," or Mexican dried beans, since these constitute the main source of calcium and phosphorus, respectively, in the average diet of a large majority of the poorer Mexican classes. We will refer to this in detail later.

In regard to the exposure to the sun, the histories contained a careful inventory of the amount of time daily that the mothers were accustomed to spend outdoors, and in the direct sunshine during pregnancy, especially during the latter half of pregnancy. Numerous questions were asked to enable us to make as accurate an evaluation of data as is possible from a retrospective history of this kind, as, for instance: Were sun baths taken? Does the mother enjoy staying in the sunshine, or does she prefer to sit and walk in the shade when outdoors? Was there available a sunporch or garden? Was the home urban or suburban?

Exposure to the Sun.—The standard used for the evaluation of the maternal exposure to sun during pregnancy was modified from that of Eliot (1925). The amount of direct exposure to sun was indicated as "good," "fair" or "poor," "good" meaning a moderate (one or two hours) or long regular daily direct exposure throughout pregnancy, taken with or without light clothing; "fair," either a

moderate direct exposure irregularly taken or a short, daily direct exposure plus a moderate or long indirect exposure, i. e., exposure to skyshine, and "poor," little or no direct exposure.

Prenatal Physical Work.—The standard used for the evaluation of physical work done by the mother was adapted from the one used by the Children's Bureau in the New Haven neonatal study. The amount of physical work was indicated as "heavy," "moderate" or "light," "heavy" meaning all the housework in a large family done by the mother; "moderate," help with the heavy housework, and "light," little or no housework.

Rest During Pregnancy.—The amount of rest and sleep during pregnancy was qualified as "adequate" or "inadequate," "adequate" meaning at least eight hours' sleep at night plus a daily nap or rest period of at least one to two hours (Davison) and "inadequate" meaning anything less than that amount.

It is obvious that in an attempt to follow arbitrary standards of this kind generalizations cannot always be made, and numerous factors have to be considered in each individual case for an adequate evaluation of data obtained.

Maternal Antepartum Diet.—The evaluation of the adequacy of the maternal antepartum diet was made with respect to the calcifying factors alone. The estimate was based mainly on the amount of milk consumed daily throughout the pregnancy. We felt that such an evaluation would be the most accurate one, first, because the intake of milk, frequently parelleling the income of the family, is usually less subject to variation than that of any other food, as a result of which a retrospective history in regard to it is more readily obtained; secondly, because milk and its products are considered to be the best source of calcium (Orr; McCollum and Simmonds; Bernheim; Gunderson), and thirdly, because the amount of calcium and phosphorus in the milk is readily estimated, 1 quart (0.94 liter) of milk being approximately equivalent to 1.2 Gm. of calcium and 0.9 Gm. of phosphorus (Garry and Stiven; Sherman). Moreover, the consensus is that from 70 to 80 per cent of the calcium contained in the diet is obtained through milk, and unless milk or cheese is included, excessively large quantities of other foods have to be consumed to fulfil the normal calcium need (Orr; Bernheim).

The mothers, however, were also questioned in regard to the use of other important calcium-containing foods, with special reference to cheese, vegetables and fruits (McCollum and Simmonds), since the latter two articles also appear to act as accessory calcifying factors (Lane). We felt that in spite of the difficulty of obtaining an accurate general retrospective history, we could get a fairly accurate qualitative estimate of the intake of vegetables and fruits, as here in southern California they constitute a common and relatively inexpensive food, the use of which is not so subject to seasonal variations as in the northern counties and states.

We believed at first that our standard for the evaluation of Mexican diets should be somewhat modified because of the high calcium content of the maize, or corn, "tortilla." Large quantities of calcium hydroxide are added to the maize in order to prepare a type of mixture known as the *masa del nixtamal,* from which the tortilla is made. Thus, as has been recently shown by Ramos Espinosa (1935), 100 Gm. of tortilla contains 0.717 Gm. of calcium in the form of calcium oxide. The average tortilla, a number of which are eaten universally by the native Mexicans at each meal in place of bread, contains on the average 0.07 to 0.12 Gm. of calcium. The tortilla, together with the "frijol" or the

Mexican dried bean, which is rich in phosphorus (Ramos Espinosa [1936*b*]), constitutes the main diet among the poor Mexican classes. However, we abandoned our original plan of estimating the calcium content of the tortilla because the dietary habits of the Mexicans in California have become somewhat modified. Few of the Mexican mothers in our study had used the lime-treated corn tortilla with any regularity, the majority having used instead the white flour tortilla, in the preparation of which no calcium is used.

As may be seen from the foregoing paragraphs, special emphasis was laid in the inquiry and in the evaluation of diets on the calcium-containing foods rather than on those containing phosphorus, for, as Sherman pointed out some years ago, the average American diet is deficient in calcium more often than in any other chemical element. It would appear that the phosphorus requirements are much more readily fulfilled and that a diet which is sufficient in calcium is almost certain to be sufficient in phosphorus as well.

In choosing our dietary standard we adhered to the most widely accepted views regarding the calcium and phosphorus requirements during pregnancy (McCollum and Simmonds; Garry and Stiven; Schwarz; League of Nations). Toverud's standard (Toverud and Toverud) was also followed as closely as possible because of the attempt made by us to compare our respective results on the relation of the maternal diet during pregnancy to the calcification of the infant's skull. It is now generally considered an established fact that during pregnancy, especially during the latter part, the calcium requirement is increased from the normal standard requirement for women of about 0.68 Gm. per day to 1.3 to 1.8 Gm., while the phosphorus requirement is increased from 1.23 Gm. per day to 1.7 to 2.2 Gm. (Garry and Stiven).

In deciding on the standard which is to be described presently, we likewise took into consideration the recent work of Coons and her co-workers on the mineral metabolism of southern women. These investigators brought out, by means of balance experiments, that an adequate retention was readily obtained even with a mean intake of 1.4 Gm. of calcium and 1.6 Gm. of phosphorus. This was ascribed by them to the influence of sunshine.

A three category, qualitative scale was thus devised to show the adequacy of each subject's diet in regard to calcifying factors, as follows: A "good" diet which was one which included either (*a*) a minimum daily intake of 1 quart (0.94 liter) or more of milk, regardless of the amount of other calcium-containing foods, or (*b*) a minimum of 1½ pints (0.71 liter) of milk plus a regular high daily intake of vegetables and fruits or a daily intake of cheese. A "fair" diet was one which included from 1 to 1½ pints (0.47 to 0.71 liter) of milk with the above exception. A "poor" diet was one which included less than 1 pint (0.47 liter) of milk a day.

Cod liver oil was not considered to be a requirement under the prevailing climatic conditions of Los Angeles.

A good diet according to our standard would contain not less than the minimum calcium and phosphorus requirements of pregnancy, as indicated previously. One must, however, realize the limitations and to some extent the inadequacy of the present dietary standards, especially in regard to the calcium and phosphorus requirements (Coons; Garry and Stiven), as well as the difficulty of evaluating with any degree of accuracy the maternal antepartum diet. The reasons for this are manifold, for example, (1) the difficulties encountered in performing balance experiments and the limited number of such experiments; (2) the multi-

plicity of factors involved in the absorption and utilization of calcium and phosphorus and (3) the difficulty in obtaining accurate retrospective histories of the diets.

One must also realize that an adequate calcium and phosphorus intake does not assure an adequate utilization of these elements, which depends chiefly on two factors—namely, the presence of vitamin D and the function of the endocrine glands (Aub; Wagoner; Gubner; Maxwell). Factors of great, though secondary, importance are the reaction of the gastric and intestinal contents (Hamilton and Moriarty), the calcium-phosphorus ratio (Garry and Stiven; Wagoner), the acid-base value of foods (Hamilton and Moriarty; Aub; Macy) and the amount of fats, cereals or oxalates in the diet (Maxwell; Wagoner; Bernheim). Much less attention than formerly is now being paid to the form, or chemical combination, in which the calcium and phosphorus are found in the food (Sherman). When one considers also the state of health of the person, the variation in the individual metabolic needs, the state of the calcium and phosphorus storage (Coons and Blunt; Rector; Dieckmann; Aub), the complex interrelation of the factors mentioned and of many that are yet unknown, one fully realizes the complexity of the subject and the limitations of our dietary standards, as well as the difficulty of drawing conclusions from such uncontrolled material as ours. However, we believe that some general trends with regard to the relation between the mother's diet and the development of cranial softening may here be brought out, since we had a fairly large series of cases and since the data had been gathered with utmost care.

CLASSIFICATION OF RESULTS [2]

The reliability of the results obtained was determined by the application of the critical ratio and the Chi square tests.[3]

The following terms were used in the interpretation of the results of the statistical analysis: "significant," indicating differences having a critical ratio of three or more times their standard error (Fisher) and in the Chi square test a P (probability) value of below 0.05; "suggestive," indicating a critical ratio of between 2 and 3; "nonsignificant," indicating a critical ratio of less than 2 or a value of P of 0.05 or greater.

INCIDENCE

Among 791 infants remaining after the exclusion of 9 for various reasons from the total series of 800, the distribution according to "hard" and "osteoporotic" skulls defined according to the standard previously described was as follows: 67.4 per cent belonging to the hard skull category and 32 per cent to the osteoporotic. Of the latter, 25.1 per cent of the total number of infants belonged to the transitional and 7.5 per cent to the soft skull group. The probable error of these per cent values was so small as to enable us to assume that the sample in the study was large enough to represent the distribution of the total population (table 2).

Among the 258 infants with cranial softening, the right parietal bone was affected alone in 54, or 29 per cent, the left alone in 26, or

2. Numerous tables pertaining to the results of the investigation had to be omitted because of lack of space. They may be obtained from us.

3. For detailed procedures in applying the Chi square test and the critical ratio, the reader may refer to Fisher.

10.1 per cent, and both bones in 178, or 69.0 per cent. These results are essentially in accord with those obtained by Hughes, who also observed a predilection for the right parietal bone and considered this fact of interest in connection with the lower life of that bone, so far as gravitation is concerned, in first positions. In his series of 76 infants, the right parietal bone alone was affected in 27, or 35 per cent, the left in 13, or 17 per cent, and both bones in 36, or 48 per cent.

TABLE 2.—*Distribution of Hard and Osteoporotic (Transitional plus Soft) Skulls in the Present Investigation as Compared to That of Toverud*

Type of Skull	Los Angeles			Oslo, Norway		
	Number	Percentage	Sigma Mean	Number	Percentage	Sigma Mean
Hard	533	67.5	1.68	61	30.5	3.25
Transitional	197	25.0	1.55	102	51.0	3.51
Soft	59	7.5	0.94	37	18.5	2.75
Total	789	100.0		200	100.0	
Transitional plus soft	256	32.5	1.68	139	69.5	3.25

TABLE 3.—*Distribution of Hard and Osteoporotic (Transitional plus Soft) Skulls by Sex*

Type of Skull	Total		Hard, Transitional and Soft Skulls				Hard and Osteoporotic (T. and S.) Skulls			
			Male		Female		Male		Female	
	No.	Per Cent Distribution	No.	%	No.	%	No.	%	No.	%
Distribution of sex in relation to total population	789	100.0	435	100.0	354	100.0	435	100.0	354	100.0
Hard	532	67.5	290	66.7	242	68.3	290	66.7	242	68.3
Transitional	198	25.0	106	24.4	92	26.0	145	33.3	112	31.7
Soft	59	7.5	39	8.9	20	5.7				

RELATION TO VARIOUS FACTORS IN INFANTS

1. Sex.—Of the 791 infants 52.2 per cent were boys and 47.8 per cent girls. Table 3 illustrates the per cent distribution of hard, transitional and soft skulls by sex. The slight preponderance of soft skulls in the boys, 8.9 per cent as compared with 5.7 per cent in the girls, was statistically nonsignificant (table 4).

2. Race.—Of the 791 infants 61.4 per cent belonged to the white racial category, 31.9 per cent to the Mexican and 6.7 per cent to the Negro. Table 5 and chart 1 clearly show the percentage distribution of hard and osteoporotic skulls by race. The results indicate a maximum incidence of cranial softening in the Negro infants and a minimum in

TABLE 4.—*Critical Ratio Test for Significance of Difference in Distribution of Hard and Osteoporotic (Transitional Plus Soft) Skulls in Relation to Certain Variables*

	Variables		Skull Type	Per Cent of Cases	No. of Cases	Variables		Skull Type	Per Cent of Cases	No. of Cases	Critical Ratio
I Infant factors	Anomalies, congenital	Present	Hard	12.9	536	Anomalies, congenital	Present	T. plus S.	21.3	258	2.86
		Present	Hard	12.9	536		Present	Soft	23.7	59	1.89
		Absent	T. plus S.	30.3	670		Present	T. plus S.	44.4	124	2.94
	Anterior fontanel	Large	Hard	64.1	181	Anterior fontanel	Small	Hard	72.4	221	1.77
		Large	Soft	11.6	181		Small	Soft	5.4	221	2.18
	Breast engorgement	Absent	Hard	9.0	536	Breast engorgement in infant	Absent	T. plus S.	12.4	258	1.42
	Conical chest	Present	Hard	13.2	536	Conical chest	Present	Soft	27.1	59	2.33
		Present	Hard	13.2	536		Present	T. plus S.	17.8	258	1.64
	Cranial sutures	Separated	Hard	15.8	536	Cranial sutures	Separated	T. plus S.	23.6	258	2.53
		Soft	Hard	4.1	536		Soft	Soft	32.2	59	4.56
		Soft	Hard	4.1	536		Soft	T. plus S.	19.4	258	5.77
	Facial asymmetry	Present	Hard	4.0	536	Facial asymmetry	Present	Soft	20.3	59	3.08
		Present	Hard	4.0	536		Present	T. plus S.	12.4	258	3.77
	Head circumference (occipitofrontal) at birth	Large	Hard	84.4	256	Head circumference	Average	Hard	65.0	323	5.56
		Average	Hard	65.0	323		Small	Hard	51.2	215	2.86
		Large	Hard	84.4	256		Small	Hard	51.2	215	7.92
		Large	Soft	1.2	256		Average	Soft	8.7	323	4.26
		Average	Soft	8.7	323		Small	Soft	13.0	215	1.52
		Large	Soft	1.2	256		Small	Soft	13.0	215	4.92
		Large	T. plus S.	15.6	256		Average	T. plus S.	35.0	323	5.74
		Average	T. plus S.	35.0	323		Small	T. plus S.	48.8	215	3.21
		Large	T. plus S.	15.6	256		Small	T. plus S.	48.8	215	8.16
	Length at birth	Large	Hard	30.2	533	Length of infant	Large	Soft	13.6	59	3.38
		Small	Hard	17.8	533		Small	Soft	25.4	59	1.29
		Large	Hard	30.2	533		Large	T. plus S.	23.5	256	2.02
		Small	Hard	17.8	533		Small	T. plus S.	25.4	256	2.38
	Molding	Present	Hard	39.1	355	Molding	Present	Soft	17.5	40	3.30
		Present	Hard	39.1	355		Absent	T. plus S.	23.1	173	3.86
	Presentation	Head	Hard	66.6	773	Presentation	Breech	Hard	100.0	24	19.5
	Race	White	Soft	7.8	486	Race	Mexican	Soft	4.8	252	1.78
		White	Soft	7.8	486		Negro	Soft	17.0	53	1.70
		Mexican	Soft	4.8	252		Negro	Soft	17.0	53	2.23
		White	T. plus S.	32.9	486		Negro	T. plus S.	49.0	53	2.23
		Mexican	T. plus S.	28.6	252		Negro	T. plus S.	49.0	53	2.74

	Sex	Male	Soft	8.9	435	Sex	Female	Soft	5.7	354	1.86
	Weight at birth	Large	Hard	81.3	193	Weight at birth	Average	Hard	64.9	399	4.39
		Large	Hard	81.3	193		Small	Hard	57.8	192	5.14
		Large	Transitional	16.1	193		Average	Transitional	27.1	399	3.15
		Large	Transitional	16.1	193		Small	Transitional	30.7	192	3.29
		Large	Soft	2.6	193		Average	Soft	8.0	399	3.03
		Large	Soft	2.6	193		Small	Soft	11.5	192	3.44
II Maternal factors	Diet	Good	Hard	30.8	146	Diet	Good	T. plus S.	33.3	180	0.48
		Poor	Hard	42.5	146		Poor	T. plus S.	30.0	180	2.34
		Good	Hard	30.8	146		Poor	Hard	42.5	146	2.09
		Good	T. plus S.	33.3	180		Poor	T. plus S.	30.0	180	0.67
	Hyperemesis during pregnancy	Present	Hard	17.7	153	Hyperemesis	Present	T. plus S.	23.5	183	1.31
	Order of birth	First	Hard	35.9	148	Order of birth	First	T. plus S.	44.6	186	1.61
		Second	Hard	18.9	148		Second	T. plus S.	29.1	186	2.20
		Fourth	Hard	13.5	148		Fourth	T. plus S.	3.7	186	3.12
	Order of birth in relation to birth interval	Second	Hard	28.5	84	Order of birth in relation to birth interval	Second	T. plus S.	61.1	80	4.43
		Third	Hard	28.5	84		Third	T. plus S.	14.9	80	2.14
		Fourth-twelfth	Hard	43.0	84		Fourth-twelfth	T. plus S.	24.0	80	2.66
	Parity	Primiparas	Hard	35.6	149	Parity	Primiparas	T. plus S.	44.6	186	1.69
	Rest	Inadequate	Hard	9.2	120	Rest	Inadequate	T. plus S.	17.4	121	1.89
	Sun exposure	Good	Hard	74.0	127	Sun exposure	Good	Soft	56.0	34	1.98
		Good	Hard	74.0	127		Good	T. plus S.	61.1	131	2.23
		Poor	Hard	9.5	127		Poor	T. plus S.	19.8	131	2.36
	Sun exposure, white mothers	Good	Hard	83.5	67	Sun exposure, white mothers	Good	T. plus S.	62.5	88	2.82
		Poor	Hard	7.5	67		Poor	T. plus S.	18.2	88	2.05
	Teeth	Good	Hard	57.2	70	Teeth	Good	T. plus S.	33.3	30	1.84
		Poor	Hard	21.4	70		Poor	T. plus S.	33.4	30	1.22
III Seasonal incidence	Incidence	Winter	T. plus S.	40.3	114	Incidence	Summer	T. plus S.	23.8	303	3.15
		Fall	T. plus S.	40.1	247		Spring	T. plus S.	31.2	125	1.69
		Fall	T. plus S.	40.1	247		Summer	T. plus S.	23.8	303	4.07
		Spring	T. plus S.	31.2	125		Summer	T. plus S.	23.8	303	1.53
		Spring	Soft	4.8	125		Fall	Soft	11.0	247	2.23
		Summer	Soft	5.0	303		Fall	Soft	11.0	247	2.55
		Winter plus fall	T. plus S.	40.2	361		Spring plus summer	T. plus S.	25.9	428	4.24
			Soft	10.5	361			Soft	4.9	428	2.91

TABLE 5.—*Distribution of Hard and Osteoporotic (Transitional Plus Soft) Skulls by Race*

	Hard, Transitional and Soft Skulls								Hard and Osteoporotic (T. and S.) Skulls					
	Total		White		Mexican Mestizo *		Negro		White		Mexican		Negro	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Distribution of racial groups in relation to total population.....	791	100.0	486	61.04	252	31.9	53	6.7	486	61.4	252	31.9	53	6.7
Distribution of groups by race.....	791	100.0	486	100.0	252	100.0	53	100.0	486	100.0	252	100.0	53	100.0
Type of skull														
Hard.....	533	67.4	326	67.1	180	71.4	27	51.0	326	67.1	180	71.4	27	5.1
Transitional.....	199	25.1	122	25.1	60	23.8	17	32.0	160	32.9	72	28.6	26	4.9
Soft.....	59	7.5	38	7.8	12	4.8	9	17.0						

* The Mexican group consisted almost entirely of Mexican Mestizos.

the Mexican, the white occupying an intermediate position. The slight predominance of osteoporotic skulls in the white as compared with the Mexican proved to be statistically nonsignificant. On the other hand, the predominance of osteoporotic skulls in the Negro as compared with the other two racial groups was statistically suggestive (tables 4 and 6). It is possible that the inconclusiveness of the results in the presence of such relatively large differences may be due to the small number of subjects in the Negro group.

We have found no other data on the racial incidence of congenital cranial softening available for comparison, although many investigators (Moore and Dennis), among them Eliot and Park, Hess (1929) and Schwarz, have noted the greater frequency of the postnatal, or so-called true, craniotabes in Negro infants. Schwarz reported that craniotabes occurred in 39.2 per cent of Negro infants examined during the first

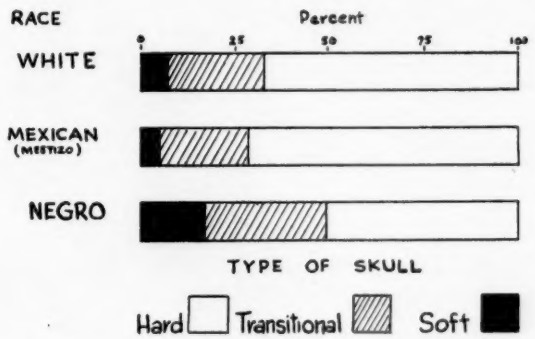

Chart 1.—Incidence of hard and of osteoporotic skulls among infants of various racial groups.

year of life, as compared with a maximum incidence of 19 per cent and a minimum of 11.5 per cent in other races. We should point out in this connection that since some of those infants were examined for the first time a few weeks after birth it is highly probable that in some cases the congenital form of cranial softening might have been present too, as differential diagnosis between the two forms of craniotabes in very young infants is difficult and often impossible unless the infant has been observed since birth.

3. Birth Weight.—The incidence of hard and of osteoporotic skulls was determined for each of the corresponding weight groups designated as "large," "average" and "small," according to the standard previously described. It may be readily seen from table 7 and chart 2 that osteoporotic skulls occur more frequently in the small than in the average or large infants, whereas the opposite is true for hard skulls. In other

TABLE 6.—*Results of Application of Chi Square Test for Significance of Relation Between Congenital Cranial Softening and Other Variables*

Variables Tested for Relationship		Skull Categories: Hard, Transitional and Soft			Skull Categories: Hard and Osteoporotic (T. and S.)		
Variables	Categories	x^2 Value	P Value	Inference	x^2 Value	P Value	Inference
Anterior fontanel (size)...	Large, average, small.....	8.6909	0.05–0.10	Nonsignificant	3.6200	0.1–0.2	Nonsignificant
Congenital anomalies.....	Present, absent.....	9.7565	0.01	Significant	9.4279	0.01	Significant
Conical chest.....	Present, absent.....	8.1753	0.01–0.02	Significant	2.9100	0.05–0.1	Nonsignificant
Facial asymmetry.....	Present, absent.....	26.4922	0.01—	Significant	18.9125	0.01	Significant
Head circumference.....	Large, average, small.....	27.3794	0.01—	Significant	21.6930	0.01	Significant
Length.....	Large, average, small.....	14.2493	0.01—	Significant	7.6079	0.02–0.05	Significant
Maternal age, primiparas.	15, 20, 25, 30, 35, 40, 45.....	13.9700	0.8+	Nonsignificant	7.3200	0.9+	Nonsignificant
Maternal age, multiparas.	15, 20, 25, 30, 35, 40, 45.....	10.8200	0.9+	Nonsignificant	5.5700	0.98	Nonsignificant
Molding.....	Present, absent.....	14.0780	0.01—	Significant	13.3446	0.01—	Significant
Parity.....	Primiparas, multiparas.....	3.5738	0.1–0.2	Nonsignificant	2.8118	0.1–0.5	Nonsignificant
Presentation.....	Cephalic, breech.....	10.8715	0.01—	Significant	10.8715	0.01—	Significant
Rest.....	Adequate, inadequate.....	3.6129	0.1–0.2	Nonsignificant	3.5032	0.1–0.5	Nonsignificant
Seasonal variation.....	Winter plus fall, spring plus summer.....	22.2370	0.01—	Significant	25.1038	0.01—	Significant
Seasonal variation.....	Winter, spring, summer, fall..	22.9898	0.01—	Significant	20.3308	0.01—	Significant
Sun exposure.....	Good, fair, poor.....	7.2802	0.1–0.2	Nonsignificant	6.5776	0.01–0.02	Significant
Sutures.....	Separated, approximated.....	8.3960	0.01–0.02	Significant	7.0351	0.01	Significant
Teeth, maternal.....	Good, fair, poor.....	8.8375	0.05+	Nonsignificant	4.7618	0.1+	Nonsignificant
Weight.....	Large, average, small.....	28.1452	0.01—	Significant	26.1601	0.01—	Significant

TABLE 7.—*Distribution of Hard and Osteoporotic (**Transitional Plus Soft**) Skulls by Birth Weight of Infant*

	Total		Hard, Transitional and Soft Skulls						Hard and Osteoporotic (T. and S.) Skulls					
			Large		Average		Small		Large		Average		Small	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Distribution of weight groups in relation to total population.....	784	100.0	193	24.6	399	50.9	192	24.5	193	24.6	399	50.9	192	24.5
Distribution of weight groups.....	784	100.0	193	100.0	399	100.0	192	100.0	193	100.0	399	50.9	53	100.0
Type of skull														
Hard.....	527	67.3	157	81.3	259	64.9	111	57.8	157	81.3	259	64.9	111	57.8
Transitional.....	198	25.2	31	16.1	108	27.1	59	30.7	36	18.7	140	35.1	81	42.2
Soft.....	59	7.5	5	2.6	32	8.0	22	11.5						

words, a definite inverse relation is demonstrated between the degree of cranial softening and the infant's birth weight, a relation proved to be statistically significant (tables 4 and 6). These results are in accord with those of Wieland, Abels and Karplus, Arluk, Toverud (1932), and Garrahan and Traversaro, who have also observed a greater incidence of congenital cranial softening in infants of lower weight groups.

In regard to the mean weights of infants belonging to the various skull type groups, the same inverse relation between birth weight and the degree of cranial softening is demonstrated. Thus, the mean weights for infants with hard, with transitional and with soft skulls were found to be 7.70 pounds (3,492.7 Gm.), 7.18 pounds (3,256.8 Gm.), and 7.12 pounds (3,229.6 Gm.), respectively. The differences in mean weight between those with hard and those with either transitional or soft skulls were statistically significant, the critical ratios being 6.62 and 5.62 respectively.

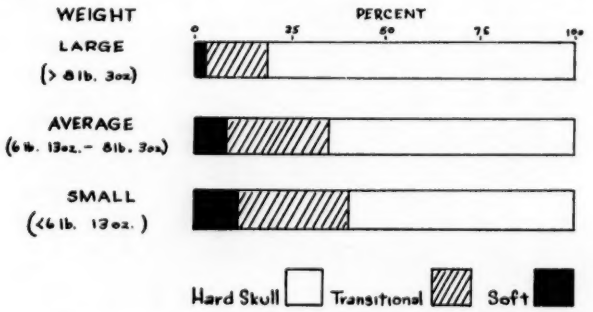

Chart 2.—Incidence of hard and of osteoporotic skulls in relation to birth weight of infant.

With respect to parity, the mean weight was 7.24 pounds (3,284 Gm.) for first-born infants as compared with 7.56 pounds (3,429.2 Gm.) for those born later, the difference between these means being statistically suggestive (critical ratio, 2.84).

In regard to race, the mean weight was 7.56 pounds (3,429.2 Gm.) for the white infants, 7.59 pounds (3,442.8 Gm.) for the Mexican and 7.25 pounds (3,288.5 Gm.) for the Negro, indicating that the mean weight of Negro infants is somewhat lower than that of the white or Mexican. The slight difference in mean weight between white and Mexican infants was statistically insignificant. The differences in mean weight between the Negro and each of the other racial groups were suggestive.

A similar observation has been made by other investigators, among them Williams, Riggs and Bivings, who found Negro infants generally smaller at birth than white infants. Bivings interpreted this to mean

TABLE 8.—*Distribution of Hard and Osteoporotic (Transitional Plus Soft) Skulls by Birth Length of Infant*

	Total		Hard, Transitional and Soft Skulls						Hard and Osteoporotic (T. and S.) Skulls					
			Large		Average		Small		Large		Average		Small	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Distribution of length groups in relation to total population	792	100.0	211	26.7	418	52.8	163	20.5	211	26.7	418	52.8	163	20.5
Distribution of groups by length	792	100.0	211	100.0	418	100.0	163	100.0	211	100.0	418	100.0	163	100.0
Type of skull														
Hard	536	67.7	151	71.6	289	69.2	96	58.9	151	71.6	289	69.2	96	58.9
Transitional	197	24.9	53	25.1	92	22.0	52	31.9	60	28.4	129	30.8	67	41.1
Soft	59	7.4	7	3.3	37	8.8	15	9.2						

that an inadequate amount of ultraviolet radiations is received by the mother during pregnancy because of the filtering action of the heavy pigmentation of the skin of the Negro on these rays.

4. Length at Birth.—Table 8 and chart 3 show the per cent distribution of hard and osteoporotic skulls within the corresponding length groups, designated according to previously described standards. An inverse relation between the degree of cranial softening and the crown-heel length at birth as well as the weight was demonstrated. The degree of relationship, however, was not so great as in the case of weight. The differences in distribution, though apparently significant according to the Chi square test (table 6), appear only suggestive when the critical ratio is used (table 4).

In regard to the mean lengths of infants of the corresponding skull type groups, the same inverse relation between the length at birth and

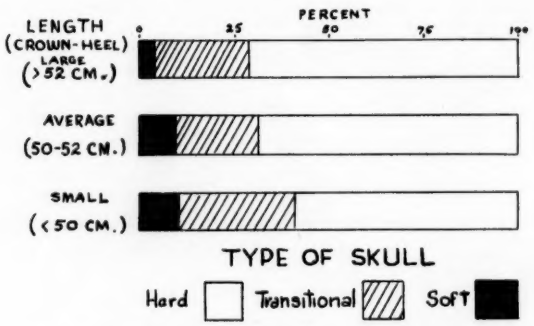

Chart 3.—Incidence of hard and of osteoporotic skulls in relation to length of infant at birth.

the degree of cranial softening is demonstrated. Thus the mean lengths for infants with hard, transitional and soft skulls were found to be 51.5 cm., 51.0 cm. and 50.7 cm., respectively. The corresponding difference in length between those with hard and those with transitional skulls was statistically suggestive, with a critical ratio of 2.36, the other differences being nonsignificant.

In regard to race, the mean lengths were as follows: 51.4 cm. for the white infants, 51.3 cm. for the Mexican and 50.8 cm. for the Negro, indicating that the mean birth length of Negro infants is somewhat lower than that of the white or Mexican. The only difference, however, which statistically was at all suggestive, having a critical ratio of 2.33, was that between the mean values of the white and the Negro infants, the rest of the differences being nonsignificant.

5. Head Circumference.—Table 9 and chart 4 show the percentage distribution of hard and osteoporotic skulls within the corresponding

TABLE 9.—*Distribution of Hard and Osteoporotic (Transitional Plus Soft) Skulls by Occipitofrontal Head Circumference of Infant*

	Total		Hard, Transitional and Soft Skulls						Hard and Osteoporotic (T. and S.) Skulls					
			Large		Average		Small		Large		Average		Small	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Distribution of groups by head circumference in relation to total population	794	100.0	256	32.3	323	40.6	215	27.1	256	32.3	323	40.6	215	27.1
Distribution of groups by head circumference	794	100.0	256	100.0	323	100.0	215	100.0	256	100.0	323	100.0	215	100.0
Type of skull														
Hard	536	67.5	216	84.4	210	65.0	110	51.2	216	84.4	210	65.0	110	51.2
Transitional	199	25.1	37	14.4	85	26.3	77	35.8	40	15.6	113	35.0	105	48.8
Soft	59	7.4	3	1.2	28	8.7	28	13.0						

occipitofrontal head circumference groups designated in accord with the previously described standards. As in the case of weight and length, a definite inverse relation with the occipitofrontal head circumference is demonstrated. The relationship is even more outstanding than in the case of birth weight, as judged by the magnitude of the actual differences in distribution and the high degree of statistical significance obtained (tables 4 and 6). Here again, as in the case of birth length, we have found no similar data in the literature to use for comparison.

In regard to the mean head circumferences of infants belonging to the respective skull type groups, the same inverse relation between the degree of cranial softening and the occipitofrontal head circumference is demonstrated. Thus, the mean head circumferences of infants with hard, with transitional and with soft skulls were 34.3 cm., 33.7 cm. and 33.4 cm., respectively, the corresponding differences between the

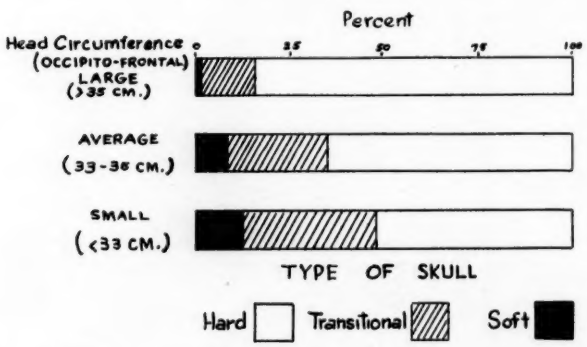

Chart 4.—Incidence of hard and of osteoporotic skulls in relation to the occipitofrontal head circumference of the infant at birth.

mean for those with hard skulls and that for infants with either the transitional or the soft type being statistically significant and the critical ratios being 6.39 and 6.68, respectively.

In regard to race, the mean head circumferences were as follows: 34.15 cm. for the white infants, 34.11 cm. for the Mexican and 33.7 cm. for the Negro, indicating that the mean head circumference of Negro infants is somewhat lower than that of the white or Mexican, the corresponding differences being statistically suggestive and the critical ratios being 2.32 and 2.05, respectively.

A similar observation has been made by Riggs and by Williams, who found that the size of the head as well as other measurements is smaller in the Negro infants at birth.

6. Size of the Anterior Fontanel.—The incidence of hard and of osteoporotic skulls was determined in relation to the size of the anterior fontanel, according to which the infants were divided into three groups as previously described. It may be seen from table 10 that there appears

TABLE 10.—*Distribution of Hard and Osteoporotic (Transitional Plus Soft) Skulls by Size of the Anterior Fontanel*

	Total		Hard, Transitional and Soft Skulls						Hard and Osteoporotic (T. and S.) Skulls					
			Large		Average		Small		Large		Average		Small	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Distribution of groups by size of anterior fontanel in relation to total population	782	100.0	181	23.1	380	48.6	221	28.3	181	23.1	380	48.6	221	28.3
Distribution of anterior fontanel groups	782	100.0	181	100.0	380	100.0	221	100.0	181	100.0	380	100.0	221	100.0
Type of skull														
Hard	528	67.7	116	64.1	252	66.3	160	72.4	116	64.1	252	66.3	160	72.4
Transitional	197	25.1	44	24.3	104	27.4	49	22.2	44	35.9	104	33.7	49	27.6
Soft	57	7.2	21	11.6	24	6.3	412	5.4	21		24		12	

to be a slight but definite tendency for small fontanels to go with hard skulls and for large ones to go with soft skulls, the transitional occupying an intermediate position. In other words, a slight direct relation is indicated between the degree of cranial softening and the size of the anterior fontanel, though some of the differences in this distribution are nonsignificant (tables 4 and 6).

7. Other Fontanels.—The posterior fontanel was palpated at the time of examination and recorded as open or closed. Since numerous investigators have observed the association of congenital cranial softening with widely open fontanels and separated sutures, we proceeded to determine the frequency with which open or closed posterior fontanels occurred among the hard and osteoporotic skull groups. The results were for some unknown reason inconsistent, for while an open posterior fontanel was found in 27 per cent of the infants with hard skulls and 36.8 per cent of those with soft, it occurred in only 20.1 per cent of the transitional groups, or in 24 per cent of the latter two groups combined. It may, however, be conluded that no correlation between congenital cranial softening and an open or closed posterior fontanel is found, for these differences in distribution were statistically nonsignificant.

Additional fontanels, all of which were sagittal, were met with in 13 of our 800 infants, or in 1.6 per cent. Their incidence was essentially the same in all skull groups, occurring in 1.7 per cent of the infants with hard skulls, 1.5 per cent of the group with the transitional type and 0.7 per cent of those with soft skulls, or in 1.6 per cent of the latter two groups combined. These differences were statistically nonsignificant. It is interesting to note that we found a less frequent occurrence of sagittal fontanels than Adair and Scammon, who observed it in 3.27 per cent of subjects, and Lea, who found it in 4.4 per cent of his series of 500 fetuses.

8. Types of Cranial Sutures.—An attempt was made to note the character of the cranial sutures in the hard, transitional and soft skulls, as numerous investigators, among them Kassowitz, Abels and Toverud (1932) have noted the frequent association of separated sutures and soft suture edges with osteoporotic skulls. This they interpreted as a sign of defective ossification. On the other hand, Hess (1929) asserted that a softening of the bones along suture lines usually characterizes the postnatal, or acquired, craniotabes and is seldom seen in conjunction with the congenital form. Hottinger (*a*) emphasized this as a point of clinical importance, for he found an associated softening along the suture lines in every subject with the postnatal form.

Separated sutures occurred in 18.3 per cent of the total number of infants, while approximated and overriding sutures were found in the rest. The results indicate a tendency for separated sutures to predom-

inate in infants with osteoporotic skulls, as seen from the fact that they were found to occur in 15.9 per cent of the infants with hard skulls, 22.1 per cent of those with transitional and 28.8 per cent of the group with soft skulls. The corresponding differences in distribution, though apparently significant according to the Chi square test, appear only suggestive when the critical ratio is used (tables 4 and 6).

In regard to the softness of the suture edges, the sagittal suture alone was usually found to be involved in our series. Only occasionally had there been an associated softening on the lambdoid and frontal suture edges. The results indicate that soft suture edges occurred in otherwise hard skulls in only 4.1 per cent of the infants, as compared with 32.2 per cent for those with soft and 15.6 per cent for the group with transitional skulls, the corresponding differences in distribution

TABLE 11.—*Distribution and Degree of Cranial Molding Among Infants with Hard and Osteoporotic (Transitional plus Soft) Skulls*

	Total		Type of Skull									
			Hard		Transitional		Soft		Hard		Transitional Plus Soft	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Distribution of molding												
Absent.....	349	66.1	216	60.9	100	75.1	33	82.5	216	60.9	133	76.9
Present.....	179	33.9	139	39.1	33	24.9	7	17.5	139	39.1	40	23.1
Degree of molding												
Slight.....	142	26.9	110	31.0	26	19.6	6	15.0	110	31.0	32	18.5
Moderate.....	33	6.2	26	7.3	7	5.3	0	0.0	26	7.3	7	4.0
Marked.....	4	0.8	3	0.8	0	0.0	1	2.5	3	0.8	1	0.6
Total.....	528	100.0	355	100.0	133	100.0	40	100.0	355	100.0	173	100.0

between the infants with hard skulls and the latter two groups being statistically significant (table 4).

9. Cranial Molding.—The incidence as well as the degree of cranial molding was observed in relation to the degree of cranial softening. In order to compile our data from a material of uniform character, we carried out our observations on infants examined on the same postnatal day, choosing the second day, on which most of the infants in our study were examined for the first time. The degree of molding was recorded as slight, moderate or marked, this evaluation being based on purely subjective criteria of diagnosis.

It may be seen from table 11 and chart 5 that the highest incidence of molding is found in the infants with hard skulls and the lowest in those with soft, the corresponding difference being statistically significant (tables 4 and 6).

As to the character of molding, no difference was observed in relation to type of skull; in all three skull groups, infants with slight molding

outnumbered those with moderate or marked molding. So far as we know, there are no similar data available in the literature for comparison. The relation of the degree of molding to cranial softening might be a point of interest from the standpoint of susceptibility of these infants to birth injury (von Haam; Holland). The interpretation of these data will be discussed under the section headed "Comment." We might mention at this time that Garry and Stiven likewise pointed out that it is a problem of practical importance to know whether there is a difference in the degree and type of molding between infants with hard and those with soft skulls.

10. Cephalhematoma.—Cephalhematona was found in only 8 of our series of 800 infants, or in 1 per cent. The results indicate that it occurred in 0.9 per cent of those with hard and 1.5 per cent of those with transitional skulls, none being found in those with soft skulls.

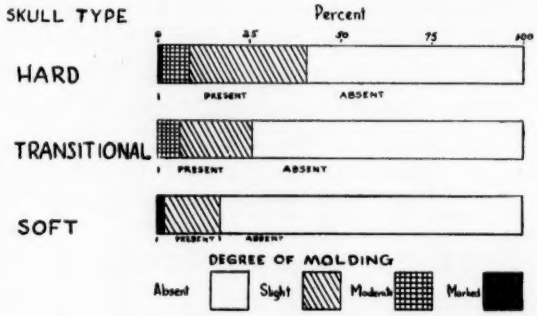

Chart 5.—Incidence of cranial molding among infants with hard and with osteoporotic skulls.

This difference was statistically nonsignificant. However, the number of infants with cephalhematoma was too small to permit us to draw any conclusions on this subject.

11. Facial Asymmetry.—By facial asymmetry we mean that type of asymmetry frequently present in the newborn, which, according to Parmelee, is due to the pressure of the shoulder against the jaw in utero. In infants with this condition there is an indentation on the corresponding side of the neck, together with a characteristic malocclusion, which consists in an overlapping of the gingival portions of the jaw on the same side and a gapping on the opposite. Because of the alleged mechanical causation of both facial asymmetry and cranial softening, we believed that it would be of interest to see whether there is any relation between the two conditions.. We therefore proceeded to observe the frequency with which facial asymmetry occurred in the

hard and the osteoporotic skull group (table 12, chart 6). The results indicate that facial asymmetry occurred five times as frequently in the infants with soft skulls and two and a half times as frequently in those with transitional, as it did in those with hard skulls, the corresponding differences in distribution being statistically significant (tables 4 and 6). In other words, a definite direct relation was observed between facial asymmetry and congenital cranial softening. The interpretation of these results will be discussed in the section headed "Comment."

12. Conical Chest.—A line of reasoning analogous to that employed in the case of facial asymmetry was followed in determining whether there is a relation between congenital cranial softening and a conically shaped chest at birth; for the latter anomaly, too, is believed by some investigators (Parmelee) to have a mechanical cause. It has been ascribed to the pressure of the arms against the anterolateral aspect

TABLE 12.—*Distribution of Facial Asymmetry Among Hard and Osteoporotic (Transitional Plus Soft) Skull Groups*

	Total		Type of Skull									
			Hard		Transitional		Soft		Hard		Transitional Plus Soft	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Total in the different skull type groups.....	794	100.0	536	100.0	199	100.0	59	100.0	536	100.0	258	100.0
Distribution of facial asymmetry												
Present.....	54	6.8	22	4.1	20	10.1	12	20.3	22	4.1	32	12.4
Absent.....	740	93.2	514	95.9	179	89.9	47	79.7	514	95.9	226	87.6

of the chest in utero. Conically shaped chest occurred in 14.7 per cent of the total number of infants. The results indicate a tendency for conical chests to predominate in the infants with osteoporotic skull, as seen from the fact that they were found to occur in 13.2 per cent of those with hard, 15.1 per cent of those with transitional and 27.1 per cent of those with soft skulls. The difference in distribution between the infants with hard and those with soft skulls is suggestive (table 4), while that between the hard skull groups and the transitional and the soft skull group combined is nonsignificant. When the Chi square test is used, the results appear significant only with a threefold classification by skull type, becoming nonsignificant when the infants with transitional and those with soft skulls are combined into one group (table 6).

13. Bowing of Tibias.—Following the same reasoning as in the case of facial asymmetry and conical chest, we proceeded to determine the degree of tibial bowing among infants of the hard and of the osteoporotic skull groups. A purely subjective criterion was used to

designate the degree of bowing as slight, moderate or marked. No relation was found between the degree of tibial bowing and the degree of cranial softening.

14. Birth Presentation.—The infants were divided according to the type of presentation into two groups, those of cephalic and those of breech presentation. Of 800 infants only 24, or 2.6 per cent, had breech presentations. Of these infants none presented even a questionable area of cranial softening. In other words, they all belonged definitely to the hard skull category. Statistically, the corresponding differences in distribution of osteoporotic skulls in infants born by the two types of presentation are significant, in spite of the small number of infants in the breech presentation group (tables 4 and 6).

A similar observation—namely, that congenital cranial softening does not occur in infants born by breech presentation—was made by

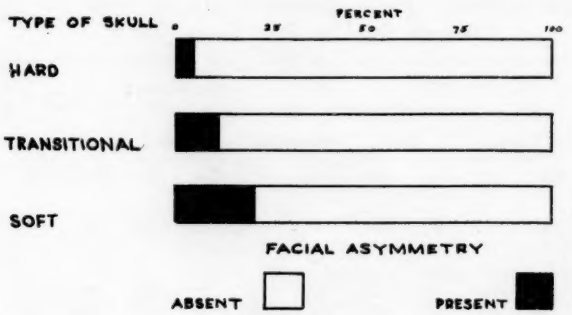

Chart 6.—Incidence of facial asymmetry among infants with hard and with osteoporotic skulls.

Hughes and by Abels and Karplus, who postulated this as their chief evidence for the mechanical causation of this anomaly. However, Toverud (1932) and Wieland maintained that congenital cranial softening may occur in infants born by breech presentation.

15. Multiple Births.—We believe that the study of congenital cranial softening in twins would contribute greatly to the understanding of its cause and pathogenesis. The reasons for this view are discussed in the section headed "Comment." Among the 800 infants there were only 5 sets of twins. All the members with the exception of 1, who had a moderate-sized area of cranial softening and therefore belonged to the transitional skull category, had hard skulls. Our results definitely show that the incidence of cranial softening is not higher in twins than in infants born at single births. If anything, the reverse appears to be the case. The number of subjects, however, is too small to enable us to draw more definite conclusions on this matter.

16. Breast Engorgement.—The incidence of breast engorgement, since its presence is considered by Parmelee as one of the most reliable criteria for judging maturity in the infant, was determined for the hard and osteoporotic skull groups. Breast engorgement was present in 90 per cent of all infants examined. No relation was found between the incidence of cranial softening and the presence or absence of breast engorgement.

17. Minute Developmental Defects and Other Congenital Anomalies.—The association of congenital cranial softening with minute developmental defects and other congenital anomalies in the infant was noted. We believed that might be a point of interest for two main reasons: (1) that minute developmental defects as well as other congenital anomalies have been looked on by many investigators (Sokolow; Bauer

TABLE 13.—*Distribution of Minute Developmental Defects and Other Congenital Anomalies Among Hard and Osteoporotic (Transitional Plus Soft) Skull Groups*

	Total		Type of Skull									
			Hard		Transitional		Soft		Hard		Transitional Plus Soft	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Congenital anomalies												
Absent.....	670	84.4	467	87.1	158	79.4	45	76.3	467	87.1	203	78.7
Present*.....	124	15.6	69	12.9	41	20.6	14	23.7	69	12.9	55	21.3
1.....	113	14.3	61	11.4	39	19.6	13	22.0	61	11.4	52	20.1
2.....	9	1.1	6	1.1	2	1.0	1	1.7	6	1.1	3	1.2
3.....	2	0.2	2	0.4	0	0.0	0	0.0	2	0.4	0	0.0
Total.....	794	100.0	536	100.0	199	100.0	59	100.0	536	100.0	258	100.0

* The numerals 1, 2 and 3 indicate the total number of anomalies in one infant.

[*a*]; Pende) as stigmas of degeneration or a constitutional inferiority and, (2) that congenital cranial softening has, too, been considered as partly due to a constitutional inferiority of the skeleton (Abels and Karplus). As minute developmental defects we designated any minor congenital anomalies, such as nevi, pilonidal sinus and anomalous-shaped auricles or digits; in other words, any minor anomaly or deviation from the norm which does not apparently interfere with the function of the affected part. Table 13 indicates that the incidence of congenital minute developmental defects plus other congenital anomalies gradually increases from the hard skull group to the soft. The differences in distribution between the total number of anomalies in the hard and the osteoporotic skull groups is statistically significant (tables 4 and 6). In regard to the frequency of multiple congenital anomalies or minute developmental defects in the various groups, the number of infants with more than one anomaly was too small to permit us to draw any conclusions

RELATION TO MATERNAL FACTORS

We wish again to point out that the results of the study of maternal and antepartum factors are based on observations conducted on a much smaller group of subjects, that is, on 341 mothers and their infants.

1. Parity.—The incidence of hard and osteoporotic skulls was observed in infants of primiparas and of multiparas. It may be seen from table 14 that a slight but definite tendency for infants with osteoporotic skulls to predominate over those with the hard is observed in offspring of primiparas as compared with multiparas. The corresponding differences, though nonsignificant according to the critical ratio, appear significant when the Chi square test is applied with a twofold classification by skull type, the two groups being (1) infants with hard skulls and (2) those of the transitional and the soft skull category combined (tables 4 and 6).

TABLE 14.—*Distribution of Hard and Osteoporotic (Transitional Plus Soft) Skulls in Infants of Primiparas and Multiparas*

	Total		Type of Skull									
			Hard		Transitional		Soft		Hard		Transitional Plus Soft	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Total in the different groups...	335	100.0	149	100.0	140	100.0	46	100.0	149	100.0	186	100.0
Primiparas...	136	40.6	53	35.6	65	46.5	18	39.1	53	35.6	83	44.6
Multiparas...	199	59.4	96	64.4	75	53.5	28	60.9	96	64.4	103	55.4

Abels and Karplus as well as Arluk and Hughes made similar observations and definitely stated that congenital cranial softening occurs with greater frequency in infants of primiparas.

2. Order of Birth.—By birth order we mean merely the order of the subject's birth with respect to the birth of siblings. In studying the order of birth in relation to congenital cranial softening, we divided the infants into five groups as follows: group I included the first born and group II the second born, the remaining groups being combined because of the small number of infants in each group. Consequently, group III included the third and fourth born; group IV the fifth, sixth and seventh, and group V the remainder, ranging from the eighth to the thirteenth born. It may be seen from table 15 that the transitional and soft skulls occur with greater frequency in the first-born and second-born infants than do the hard skulls, while the reverse is true for all of the remaining groups. The corresponding differences are statistically suggestive only when the comparison is made with a twofold classification by skull type, that is, with one group composed of infants with hard skulls and the other of those in the transitional and the soft skull

category combined. The only definitely significant difference is that found in group IV (table 4). Although there are observations available on the incidence of congenital cranial softening in infants of primiparas and of multiparas, we have found no similar data in regard to its relation to the order of birth.

Since numerous pregnancies occurring at frequent intervals are, by force of their depleting action on the maternal calcium storage, considered as a factor contributing to a postnatal predisposition of the infant to rickets (Rector; Mull and Bill; Dieckmann), we believed that it would be of interest to note whether it might also be a predisposing factor to congenital cranial softening.

The order of birth was plotted against the average interval between births for infants with hard and those with osteoporotic skulls, the

TABLE 15.—*Distribution of Hard and Osteoporotic Skulls by the Order of Birth*

	Total		Type of Skull									
			Hard		Transitional		Soft		Hard		Transitional Plus Soft	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Total in the different skull groups.....	334	100.0	148	100.0	140	100.0	46	100.0	148	100.0	186	100.0
Order of birth												
I (1st).....	136	40.7	53	35.9	65	46.4	18	39.1	53	35.9	83	44.6
II (2d).....	82	24.5	28	18.9	39	27.9	15	32.6	28	18.9	54	29.1
III (3d and 4th)	74	22.2	38	25.7	27	19.3	9	19.6	38	25.7	36	19.3
IV (5th, 6th and 7th).....	27	8.10	20	13.5	3	2.14	4	8.7	20	13.5	7	3.77
V (8th to 13th)	15	4.5	9	6.08	6	4.29	0	0.00	9	6.08	5	3.23

transitional and soft skull infants having been combined into one group because of the small number of subjects in each of these categories. The average interval between births was obtained by dividing the total number of years of childbearing, calculated from the time of the onset of pregnancy with the first-born infant to the time of the birth of the last, by the total number of births. The mothers in this series, of course, included multiparas only, the number of births ranging from two to thirteen. The corresponding table is not presented here. The results, however, indicated no apparent relation between the incidence of hard or osteoporotic skulls and either the average interval between births per se or the interval in relation to the total number of births. However, there appears to be a definite correlation with the order of birth alone, for the osteoporotic skulls tend to occur among the second-born infants more frequently than do the hard, whereas the reverse is true for the third-born infants and those born later. This is especially well illustrated if one compares the total number of infants with hard and osteoporotic skulls in each birth order group. Thus 61.1 per cent of the total

number of infants with osteoporotic skulls were found in the second birth order group, as compared with 28.5 per cent of those with the hard, the corresponding difference being statistically significant. On the other hand, the infants with hard skulls outnumbered those with osteoporotic in the remaining birth groups. The difference between the 28.6 per cent for infants with hard skulls and the 14.9 per cent for those with osteoporotic skulls found in the third birth order group was statistically suggestive, as was the corresponding difference between the 43.0 per cent for the hard skull group and the 24.0 per cent for those with osteoporotic, found in the remaining birth order groups combined (table 4). The interpretation of these results will be discussed in the section headed "Comment."

3. Maternal Age.—The incidence of congenital cranial softening was studied in relation to the maternal age. The corresponding table showing the incidence of hard and osteoporotic skulls in infants born in various maternal age intervals for primiparas and multiparas considered together and separately is not presented here. The results indicated that although the highest number of infants of all skull types is found in the 20 to 24 year age interval for the multiparas and primiparas combined, the infants with osteoporotic skulls outnumbered those with the hard in this age interval, the reverse being true for all the other age groups. Statistically none of these differences is significant (table 4).

In an attempt to see whether this trend might be explained on the basis of some possible interrelated factors, the age variation was determined for mothers of the various racial groups and for multiparas and primiparas separately. The average ages in the same classification were likewise determined. It was revealed that although the highest number of mothers in all racial groups fell in the 20 to 24 year interval and although the number of Mexican mothers exceeded the number of white and of Negro mothers in the 15 to 19 year intervals, there appeared to be no definite trend in the age variation with respect to race. The average ages for the white, the Mexican and the Negro mothers were practically the same, i. e., 24.99, 24.78 and 24.87 years, respectively, the minute differences being statistically nonsignificant.

Chart 7 shows the age variation for primiparas and for multiparas separately with respect to the type of the infant's skull. Essentially the same trend as in the age variation for primiparas and multiparas combined is shown by the multiparas alone, namely, that the infants with osteoporotic skulls outnumber those with hard skulls in the 20 to 24 year interval, whereas the reverse is true for the subsequent age intervals. A difference is presented by the 15 to 19 year interval, in which the number of infants with osteoporotic skulls slightly exceeds that of the group with hard skulls.

Almost exactly the reverse situation is observed in regard to primiparas (chart 7). Among the offspring of this group infants with hard skulls definitely outnumber those with osteoporotic in the 15 to 19 year interval, whereas the reverse occurs in all the subsequent age periods. The average maternal ages with respect to parity and the type of the infant's skull were as follows: Among primiparas the average maternal age in years was 21.46 for all the infant skull groups combined, 20.0 for the hard skull group, 22.38 for the transitional and 22.47 for the soft, or 22.4 for the transitional and soft combined. The corresponding averages for the multiparas were 27.31, 28.35, 26.01, 27.26 and 26.34 years, respectively. It may therefore be seen that among primiparas the average maternal age was two and four tenths years higher for those having infants with osteoporotic skulls than for mothers of

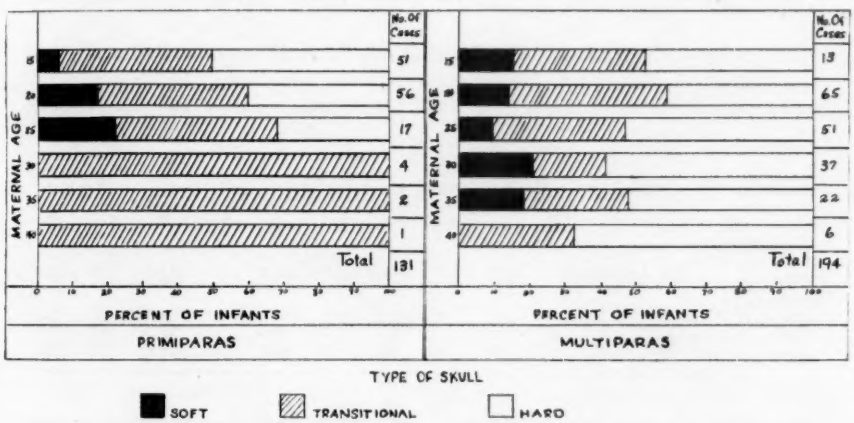

Chart 7.—Incidence of hard and of osteoporotic (transitional plus soft) skulls in relation to parity and maternal age.

infants with hard skulls, this difference being statistically significant, with a critical ratio of 3.43. On the other hand, the reverse was true for the multiparas, that is, the average maternal age was two years higher for the hard skull infants, this difference being statistically suggestive, with a critical ratio of 2.29.

It would thus appear, from the study of these tables, that the infants with osteoporotic skulls tend to occur more frequently among the offspring of the older primiparas and the younger multiparas, while the reverse is true for the infants with hard skulls. The interpretation of this finding will be discussed under the heading of "Comment."

4. Maternal Exposure to Sun During Pregnancy.—The amount of the exposure of the mother to sun during pregnancy, designated as "good," "fair" and "poor" according to the standard previously

described, was determined for the infants with hard and with osteoporotic skulls (table 16, chart 8). It may be seen that a definite, negative correlation is observed between the degree of the maternal exposure to sun during pregnancy and the degree of cranial softening. Statistically, the differences in distribution of infants with hard and osteoporotic skulls within the various sun exposure groups appear significant according to the Chi square test and suggestive according to the critical ratio, when a twofold skull type classification is used, that is, when the two groups are (1) infants with hard skulls, and (2) those with transitional and those with soft skulls combined (tables 4 and 6).

In order to ascertain further the apparent relation between the mother's exposure to sun during pregnancy and the degree of cranial softening in the infant, we proceeded to determine whether the same relation would still be noted when each racial group was considered

TABLE 16.—*Distribution of Hard and Osteoporotic (Transitional Plus Soft) Skulls in Relation to Maternal Exposure to Sun During Pregnancy*

	Total		Type of Skull									
			Hard		Transitional		Soft		Hard		Transitional Plus Soft	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Total in the different skull type groups.....	258	100.0	127	100.0	97	100.0	34	100.0	127	100.0	131	100.0
Sun exposure												
Good.....	174	67.5	94	74.0	61	62.9	19	56.0	94	74.0	80	61.1
Fair.....	46	17.8	21	16.5	17	17.5	8	23.6	21	16.5	25	19.1
Poor.....	38	14.7	12	9.5	19	19.6	7	20.4	12	9.5	26	19.3

separately. The results indicated that although the same relation was observed in the white and in the Negro group, it was not distinct in the Mexican. There was, however, too small a number of subjects in the Negro and in the Mexican racial category to enable us to draw any definite conclusions. The differences in distribution between the infants with hard and those with osteoporotic skulls in the good and the poor sun exposure groups of mothers are statistically suggestive for the white racial group, in spite of the small number of subjects in the various categories (table 4).

In the study of the character of the maternal exposure to sun in respect to the white, the Mexican and the Negro racial group, it was observed that the white had the highest incidence of good sun exposures, while the Mexican had the lowest. It may be concluded, therefore, that the racial variation in the incidence of congenital cranial softening cannot be attributed to the character of the exposure to sun in respect to these racial groups, for the least number of infants with osteoporotic skulls

was found among the offspring of the Mexicans, who had reported the least amount of exposure to sun.

5. Maternal Diet During Pregnancy.—In order to find out whether there is a relation between the calcifying factors of the mother's antepartum diet and the type of the infant's skull, the frequency distribution of "good," "fair" and "poor" diets, designated according to the standard previously described, was determined for the hard and osteoporotic skull groups (table 17). No apparent relation between the type of diet, from the standpoint of its calcifying factors, and the degree of cranial softening in the infant was revealed. In fact, there even appears to be a slight negative correlation between the type of diet and the degree of hardness of the infant's skull, as judged from the presence of a greater number of poor diets in association with the hard skull category than with the osteoporotic, as well as from the presence of a

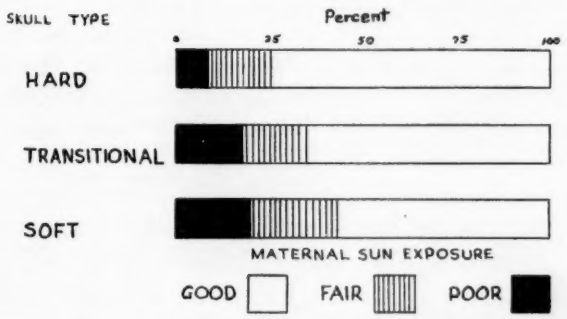

Chart 8.—Percentage of good, of fair and of poor maternal sun exposure during pregnancy, in relation to hard and to osteoporotic skull groups.

greater number of infants with hard skulls in the poor diet category than in the good, the corresponding differences being statistically suggestive (table 4). This is just the opposite from what would be expected were a calcium and phosphorus deficiency of the antepartum diet the main etiologic factor of congenital cranial softening, as claimed by Toverud (1931; 1932). Because of the complete lack of agreement between the results here obtained and those of Toverud, we proceeded to make a careful analysis of our results.

In undertaking the investigation we considered the possibility of the existence of an interrelated, contributory etiologic factor which might so mask or otherwise affect the results as actually to conceal an existing relation to the maternal diet. The first step in this investigation was to rule out the influence of race. For this purpose we proceeded to find out whether the same results were present when each racial group was

considered separately (table 18). Moreover, we believed our white racial group to be more comparable to the subjects observed by Toverud in her study, from the racial standpoint. It may be seen from table 18 that the same absence of correlation between the type of maternal diet

TABLE 17.—*Distribution of Hard and Osteoporotic (Transitional Plus Soft) Skulls in Relation to Maternal Diet During Pregnancy*

	Total		Type of Skull							
			Hard		Transitional		Soft		Hard	Transitional Plus Soft
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Total in the different skull groups	326	100.0	146	100.0	136	100.0	44	100.0	146	100.0	180	100.0
Type of diet												
Good	105	32.2	45	30.8	47	34.6	13	29.6	45	30.8	60	33.3
Fair	105	32.2	39	26.7	48	35.3	18	40.8	39	26.7	66	36.7
Poor	116	35.6	62	42.5	41	30.1	13	29.6	62	42.5	54	30.0

TABLE 18.—*Distribution of Hard and Osteoporotic (Transitional Plus Soft) Skulls in Relation to the Maternal Diet During Pregnancy in White, Mexican and Negro Populations*

				Type of Skull						
		Total		Hard		Transitional		Soft		Transitional Plus Soft
Race	Quality of Diet	No.	%	No.	%	No.	%	No.	%	No.	%
White	Good	70	35.5	28	35.4	33	37.5	9	30.0	42	35.8
	Fair	66	33.5	23	29.2	29	33.0	14	46.7	43	39.8
	Poor	61	31.0	28	35.4	26	29.5	7	23.3	33	26.4
	Total	197	100.0	79	100.0	88	100.0	30	100.0	118	100.0
Mexican (Mestizo)	Good	26	26.8	16	29.6	8	21.6	2	33.3	10	23.2
	Fair	29	29.9	10	18.5	17	46.0	2	33.3	19	44.2
	Poor	42	43.3	28	51.9	12	32.4	2	33.3	14	32.6
	Total	97	100.0	54	100.0	37	100.0	6	100.0	43	100.0
Negro	Good	9	28.1	1	7.6	6	54.5	2	25.0	8	42.1
	Fair	10	31.2	6	46.2	2	18.2	2	25.0	4	21.1
	Poor	13	40.7	6	46.2	3	27.3	4	50.0	7	36.8
	Total	32	100.0	13	100.0	11	100.0	8	100.0	19	100.0
Sum of totals		326	100.0	146	100.0	136	100.0	44	100.0	180	100.0

and the type of skull is observed. Since a racial variation in the incidence of congenital cranial softening had previously been observed, we determined the prevailing type of diet in the corresponding racial groups in order to ascertain whether this racial variation might be ascribed to the influence of diet. Table 18 shows that the best dietary conditions are found among the white group, with the next best in the Negro and the worst in the Mexican. These results would seem to speak against a dietary influence, at least from the standpoint of calcifying factors,

for the incidence of osteoporosis was found to be lowest in the Mexican infants and highest in the Negro. Moreover, these observations would also appear to indicate that the existing racial variation in the incidence of the anomaly under consideration cannot be ascribed to the influence of the maternal diet during pregnancy.

The next step in the analysis of our results was to observe the incidence of hard and of osteoporotic skulls in relation to the vegetable and fruit content of the mother's antepartum diets, assuming that a high enough intake of these foods might make up for a calcium and phosphorus deficiency due to an insufficient milk intake, on which article of food our dietary standard was mostly based. We thus proceeded to regrade the antepartum diets according to their milk content alone, "good" meaning an intake of 1 quart (0.94 liter) or more of milk per day, "fair" 1 to 1½ pints (0.47 to 0.71 liter) and "poor" less than 1 pint. We then determined the quality of the thus graded diets with respect to the vegetable and fruit content, a "high" vegetable and fruit intake meaning a daily, regular intake of one or more raw and cooked vegetables and fruits, "moderate" meaning a daily intake of some vegetable and fruit and "low" meaning an intake of little or no vegetables or fruits. Corresponding tables showing the per cent distribution of hard and osteoporotic skulls for each of the diet categories in regard to each racial group separately as well as all groups combined are not presented here. The results revealed no obvious relation between the type of diet with respect to its vegetable and fruit or its milk content and the incidence of congenital cranial softening.

Lastly, since Coons and her co-workers (1935) have shown that a lower calcium and phosphorus intake is needed to satisfy the requirements of Southern women, a fact which they attributed to the effect of sunshine, an attempt was made by us to find out whether the apparent discrepancy in our results with respect to diet might be attributed to a still greater effect of sunshine. In other words, the question was raised as to whether a satisfactory exposure to sun during pregnancy might be a factor so potent as to compensate to a great extent for a mineral dietary deficiency, especially since our results have shown that there is an apparent relation between the degree of the mother's antepartum exposure to sun and the degree of calcification of the infant's skull. We reasoned that this assumption, if true, might also explain our failure to confirm Toverud's (1931; 1932) results. This possibility being kept in mind, the distribution of infants with hard and with osteoporotic skulls in relation to the mother's diet and exposure to sun was studied for each racial group separately as well as for all three combined. The corresponding tables are not presented here. However, the results again failed to show any positive correlation between the type of diet and the degree of hardness of the infant's skull. In these figures also, a slightly

negative correlation was observed which was found to be statistically suggestive. After the reexamination of our data, we are still unable to concur with the results obtained by Toverud. We are not prepared to explain this lack of agreement in our results, considering the similarity of the dietary standard as well as of the criteria for skull classification employed in our respective studies.

6. Physical Work and Rest During Pregnancy.—An attempt was made to see whether there is a relation between the incidence of congenital cranial softening and the amount of physical work and rest during pregnancy.

A table not presented here, which showed the per cent distribution of hard and of osteoporotic skulls for the "heavy," the "moderate" and the "light" physical work group, revealed no apparent relation between the amount of physical work done during pregnancy and the degree of cranial softening.

In regard to the influence of rest during pregnancy, the results indicate that the number of infants with osteoporotic skulls is slightly higher in the "inadequate rest" category. Thus 17.4 per cent of the 121 infants with osteoporotic skulls occurred in the "inadequate rest" category, as compared with 9.2 per cent of the 120 infants with hard skulls, the corresponding difference being statistically suggestive (table 4). In other words, there appears to be a slight negative correlation between the amount of rest during pregnancy and the degree of cranial softening.

7. Hyperemesis and Toxemia of Pregnancy.—An attempt was made to determine whether certain complications of pregnancy, such as excessive vomiting or toxemia, are contributory etiologic factors of congenital cranial softening.

Vomiting was recorded as present or absent. Slight vomiting occurring only at the onset of pregnancy for not longer than about a month was disregarded. The results indicated that the frequency of vomiting was slightly greater in mothers of infants with osteoporotic skulls than in those of the infants with hard skulls, the corresponding difference, though almost suggestive, being statistically nonsignificant (table 4).

The percentage distribution of toxemia was determined for the various skull type groups. A total of 28 patients with toxemia was found among 341 mothers. Of these, 15 belonged to the group of 151 mothers of hard skull infants, and 13 to that of 185 mothers of the osteoporotic skull group. In other words, no apparent relation between the incidence of toxemia and that of congenital cranial softening was observed. If anything, the incidence of toxemia is slightly greater for the hard skull group than for the osteoporotic, the difference, however, being statistically nonsignificant (table 4).

Toverud (1932) noted the frequent association of excessive vomiting and other pathologic conditions during pregnancy with a greater incidence of congenital cranial softening in the offspring.

8. Type of Delivery.—The type of delivery was recorded as normal spontaneous and instrumental. The mothers with their infants were thus arbitrarily divided according to the type of delivery into two groups, and the percentage distributions of normal spontaneous and of instrumental deliveries were determined for the corresponding skull type groups. No obvious correlation was found between the type of delivery and congenital cranial softening. The existing slight differences were statistically nonsignificant.

9. Condition of Maternal Teeth.—Because of the existing relation of dental caries to the calcifying factors of the diet and the calcium and phosphorus metabolism in general (Toverud and Toverud; Drain, Plass and Oberst; Bloom; Carelli; Reed), we believed that it might be of interest to note also the condition of the maternal teeth with respect to caries and the association of the condition with the presence or absence of congenital cranial softening in the offspring. A rather subjective method of clinical interpretation was used to evaluate the condition of maternal teeth in terms of "good," "fair" and "poor," the age of the mother, however, being taken into consideration. The corresponding table is not presented. A slight but definite tendency for the infants with osteoporotic skulls to outnumber those with the hard among the offspring in the "fair" and "poor" teeth category was revealed. The corresponding differences are statistically nonsignificant, although almost suggestive (table 4). Because of the subjectiveness of our clinical interpretation of the condition of the maternal teeth and because of the relatively small number of subjects in this group, we believe that no definite conclusions can be drawn on this point.

10. Other Maternal Data.—In regard to the relation of congenital cranial softening to syphilis, our 14 instances of positive Wassermann reaction of the mother's blood, an incidence of 2.5 per cent in the total series of 800 infants and their mothers, are too few to enable us to draw conclusions. A positive Wassermann reaction of the blood occurred in 2.6 per cent of the mothers of the hard skull group of infants, 1.0 per cent of those of the transitional skull group and 5.1 per cent of the mothers of the infants with soft skulls, or in 1.94 per cent of the total number of mothers of infants with osteoporotic skulls. In other words, in this small group no apparent relation was noted between positive Wassermann and Kahn reactions of the maternal blood and the incidence of congenital cranial softening.

The results are likewise inconclusive when one attempts to determine whether there is a relation between congenital cranial softening and the

maternal home environment during pregnancy. The type of home environment expressed in terms of "good," "fair" and "poor" was judged subjectively from the maternal history. It was also noted whether the home was urban or suburban. We believed that this point might be of interest from the standpoint of the economic status of the patient and the availability of sunshine. No apparent relation was noted between the type of home environment and the incidence of congenital cranial softening. Although the infants with hard skulls tended to predominate slightly among the offspring of good home environment and those with osteoporotic skulls among fair environment, the corresponding differences were statistically nonsignificant.

An attempt was also made to determine whether congenital cranial softening in Mexican infants is more prevalent among offspring of native or of foreign-born mothers. We believed that this point might be of some interest because of the generally changing dietary habits of the Mexicans in California, resulting in a lower calcium intake than that of the large majority of Mexicans in most portions of Mexico. The results showed no apparent relation between the birthplace of either parent and the incidence of cranial softening in the infant. The slight difference in the frequency of osteoporotic skulls in favor of the foreign-born parents was statistically nonsignificant.

Lastly, the mothers were questioned in regard to the maternal and the paternal health at the time of conception and the maternal health during pregnancy. Our results showed a complete absence of correlation between, on the one hand, maternal and paternal health at the time of conception and the maternal state of well-being during pregnancy and, on the other, the degree or incidence of cranial softening in the offspring. We believe, however, that the results obtained in this connection are rather inconclusive, for they are based on data from the maternal history, or subjective statements alone.

It would appear to us that some of the observations in this section on maternal factors, while of no apparent positive value, may offer something in a negative sense.

IV. SEASONAL VARIATION

Because of the alleged relation of congenital cranial softening to rickets and postnatal craniotabes and the known seasonal variation of these two anomalies (Eliot; Hess [1929]; and others), an attempt was made to determine whether congenital cranial softening is likewise subject to seasonal variation.

The distribution of infants with hard and with osteoporotic skulls was studied monthly, seasonally and biyearly (table 19, chart 9). Because of the small number of infants in some of the monthly cate-

gories, the monthly variation of the incidence was not taken much into account. We believed, however, that some definite conclusions could be drawn from the seasonal variation. For this purpose the incidence of this anomaly was studied seasonally and biyearly as follows: For the seasonal study the year was divided into the accepted four trimonthly seasons, December, January and February, being taken as the winter months, March, April and May as the spring and so forth, while for the biyearly study the year was divided into two equal semesters, one

TABLE 19.—*Monthly, Seasonal and Biyearly Incidence of Hard and Osteoporotic (Transitional Plus Soft) Skulls*

		Type of Skull									
		Hard		Transitional		Soft		Total		Transitional Plus Soft	
Seasons	Months	No.	%	No.	%	No.	%	No.	%	No.	%
Autumn.....	September	48	63.2	15	19.7	13	17.1	76	100	28	36.8
	October	60	63.8	28	29.8	6	6.4	94	100	34	36.2
	November	40	51.9	29	37.7	8	10.4	77	100	37	48.1
	Total	148	59.9	72	29.1	27	11.0	247	100	99	40.1
Winter.....	December	19	48.7	14	35.9	6	15.4	39	100	20	51.3
	January	17	58.5	8	27.6	4	13.8	29	100	12	41.4
	February	32	69.6	13	28.3	1	2.1	46	100	14	30.4
	Total	68	59.6	35	30.7	11	9.7	114	100	46	40.4
Autumn plus winter.....		216	59.8	107	29.7	38	10.5	361	100	145	40.2
Spring.....	March	30	66.7	11	24.4	4	8.9	45	100	15	33.3
	April	35	66.0	17	32.0	1	2.0	53	100	18	34.0
	May	21	77.8	5	18.5	1	3.7	27	100	6	22.2
	Total	86	68.8	33	26.4	6	4.8	125	100	39	31.2
Summer.....	June	31	77.5	8	20.0	1	2.5	40	100	9	22.5
	July	105	79.5	22	16.7	5	3.8	132	100	27	20.5
	August	95	72.5	27	20.7	9	6.8	131	100	36	27.5
	Total	231	76.2	57	18.8	15	5.0	303	100	72	23.8
Spring plus summer.....		317	74.1	90	21.0	21	4.9	428	100	111	25.9
Total.....		533	67.5	197	25.0	59	7.5	789	100	256	32.5

including the fall and winter, or the cold months, and the other the spring and summer, or the warm months. It may be readily seen from an inspection of table 19 and chart 9 that there are a definite seasonal and biyearly variation in the incidence of congenital cranial softening. While the highest peak for the incidence of rickets and postnatal craniotabes occurs in winter and early spring (Moore and Dennis; Hess [1931]), that for congenital cranial softening occurs in fall and winter in our series of cases. Its incidence is practically the same in fall and in winter, whereas it is definitely lower in summer than in spring. In other words, the incidence of congenital cranial softening follows inversely the curve of sunshine, and its maximum incidence precedes the peak

for rickets and the postnatal, or acquired, craniotabes by about three months. In studying the biyearly variation one may note that the incidence of osteoporotic skulls in the warm months is only half what it is in the cold. The same trend is observed when the seasonal variation is studied in the white, the Mexican and the Negro group separately.[4] Although the seasonal variation appears to be most marked in the Negro and least in the Mexican, the number of infants in these two racial groups is too small in some of the seasonal categories to permit us to draw any definite conclusions on this point.

Statistically, the seasonal variation of the incidence of congenital cranial softening is shown to be definitely significant by the use of the Chi square test (table 6). When the critical ratio is used, significance

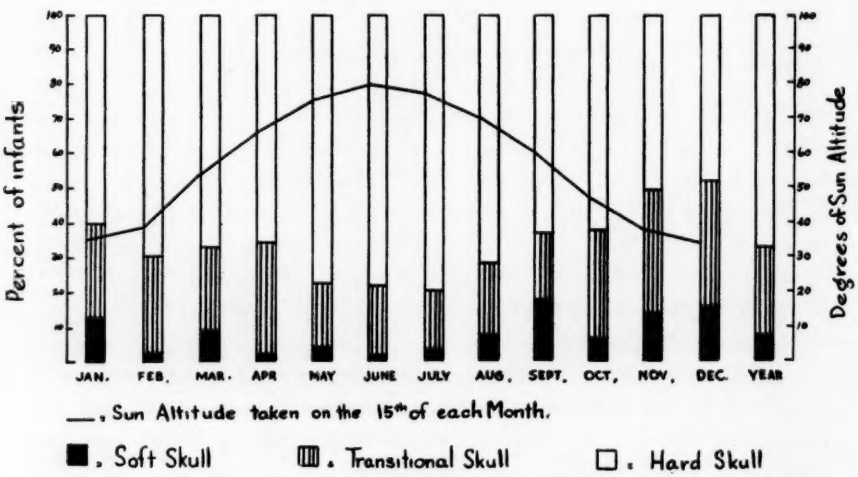

Chart 9.—Seasonal variation of the incidence of hard and of osteoporotic skulls in relation to seasonal variation of the maximum daily altitude of the sun recorded by the month.

is obtained in the four-seasonal variation, when the comparison is made with a twofold classification by skulls, that is, with the transitional and soft skull groups combined (table 4). However, not all the differences here are found to be significant. The differences in distribution of the hard and of the osteoporotic skulls for winter and fall as compared with that for summer is significant, whereas the corresponding differences between spring and the other three seasons are nonsignificant (table 4). The corresponding biyearly differences are more strikingly significant, as judged by the still higher values of their critical ratios as well as by the fact that the corresponding differences approach significance even

4. The corresponding table is not presented for lack of space.

when the transitional and the soft skull group are considered as separate categories (table 4). This would appear to indicate that the failure to obtain statistical significance in a study of four-seasonal variation when a threefold skull classification is used for comparison is probably due to the small number of subjects in some of these categories.

In studying the monthly variation of the incidence of congenital cranial softening one may note that it varies fairly closely with the curve of sunshine, as judged from the maximum daily altitude of the sun recorded by the month (chart 9). This is especially well illustrated by calculating from the yearly averages of those monthly altitude values as well as from the yearly average incidence of congenital cranial softening, considered as 100 per cent, the monthly averages of both in terms of per cent of the yearly averages (table 20). The results indicate that

TABLE 20.—*Seasonal Mean Incidence of Osteoporotic (Transitional Plus Soft) Skulls in Relation to the Mean Temperature and Seasonal Altitude of the Sun According to Their Respective Yearly Averages*

Season	Incidence of Osteoporotic (T. and S.) Skulls				Temperature, F.		Maximum Daily Altitude of Sun	
	Total No. of Skulls Observed	No. of Osteoporotic Skulls	%	% of Yearly Average	Mean Seasonal Temperature	% of Yearly Average	Mean Seasonal Altitude	% of Yearly Average
Winter	114	46	40.3	124.6	57.0	89.1	37.2	65.9
Spring	125	39	31.2	96.0	60.9	95.2	65.0	115.3
Summer	303	72	23.8	73.2	70.9	110.8	75.5	132.1
Autumn	247	99	40.1	123.4	67.4	105.0	47.8	84.7
Total for year	789	256						
Yearly average	...	...	32.5	100.0	64.0	100.0	56.4	100.0

the lowest seasonal incidence of congenital cranial softening parallels fairly closely the maximum seasonal altitude of the sun, and vice versa. The same relation is observed, although with a few exceptions, from the study of the monthly figures. The most obvious discrepancies appear to occur in the data for the months of September, when a sudden rise in the frequency of osteoporosis is observed, and February, when a sudden fall is noted (table 19, chart 9). We are not prepared at the present time to explain these apparent discrepancies in results, especially that of the sudden rise in the incidence of osteoporotic skulls in September, a month preceded by a season of optimum sunshine, as judged from the monthly and seasonal values of the maximum daily altitude of the sun (Tisdall and Brown). Nor are we prepared to explain this peculiar type of seasonal variation—peculiar because it would appear that in following so closely the curve of sunshine the incidence of congenital cranial softening is largely dependent on the quality of sunshine during the last prenatal month rather than on the total number of months of optimum sunshine during pregnancy (table 19, chart 9). Thus, for

example, the incidence in October is considerably lower than that in May, although the prenatal period of infants born in the former month has included by far a greater number of months of optimum sunshine than has that of those born in the latter.

Several other investigators have noted a seasonal variation in the incidence of congenital cranial softening. Thus, Abels and Karplus

TABLE 21.—*Comparative Data on Seasonal Incidence Variation of Congenital Cranial Softening or Osteoporosis as Given by Various Authors*

	Present Investigation (California)				Hughes' Investigation* (England)				Garrahan's Investigation† (Argentine)			
	Total Number of Skulls Observed	Number of Osteoporotic Skulls	Percentage	Percentage of Yearly Average	Total Number of Skulls Observed	Number of Osteoporotic Skulls	Percentage	Percentage of Yearly Average	Total Number of Skulls Observed	Number of Osteoporotic Skulls	Percentage	Percentage of Yearly Average
December.....	39	20	51.3	157.8	27	9	33.3	154.9	32	3	9.37	186.3
January.....	29	12	41.4	127.4	28	4	14.2	66.0	114	6	5.26	104.6
February.....	46	14	30.4	93.5	16	2	12.5	58.1	78	7	8.97	178.3
Winter.....	114	46	40.4	124.3	71	15	21.1	98.1	224	16	7.10	141.1
March.....	45	15	33.3	102.5	21	3	14.5	62.7	101	5	4.95	98.4
April.....	53	18	34.0	104.6	24	6	25.0	116.3	122	4	3.27	65.0
May.....	27	6	22.2	68.5	25	3	12.0	55.8	133	10	7.51	149.3
Spring.....	125	39	31.2	96.0	70	12	17.1	79.1	356	19	5.4	107.4
June.....	40	9	22.5	69.2	20	2	10.0	46.5	148	6	4.05	80.5
July.....	132	27	20.5	62.1	18	5	27.7	128.8	186	7	3.76	74.8
August.....	131	36	27.5	84.1	23	3	13.0	60.5	99	3	3.03	60.2
Summer.....	303	72	23.8	73.2	61	10	16.3	75.8	433	16	3.7	73.6
September.....	76	28	36.8	113.2	22	10	45.4	201.8				
October.....	94	34	36.2	111.4	19	5	31.5	146.5				
November.....	77	37	48.1	148.0	26	5	19.2	89.3				
Autumn.....	247	99	40.1	123.4	67	21	31.3	145.6				
Total for year..	789	256			269	58			1,013	51		
Yearly average.	...	...	32.5	100.0	...	..	21.5	100.0	...	..	5.03	100.0

* The values given here for Hughes' investigation were estimated from curves.
† Since the seasons in the Argentine are in reverse order from those in the United States and England, Garrahan's data from June to February were tabulated under December to August.

found winter to be the season of its maximum incidence, while Arluk placed it in winter and spring. The only numerical data, however, that we were able to find on the subject of the seasonal variation of congenital cranial softening are those of Hughes from England and those of Garrahan and Traversaro from Argentina. Unfortunately the lack of a uniform objective criterion of what constitutes a soft or osteoporotic skull makes the comparison of our results with those of these investigators limited. In other words, while we are able to compare the

degree of seasonal variation present, we are not able to compare the incidence of this condition as found in these respective localities and draw conclusions from the differences observed. In order to make our results comparable to those of these investigators a table was prepared in which the monthly incidence averages were expressed in terms of percentage of the monthly totals of all infants examined (table 21). It may be seen from this table as well as from chart 10 that a great similarity in the seasonal variation curve exists in all three studies. Unfortunately, the season corresponding to our fall season is absent from Garrahan's study. For the remaining three seasons, the seasonal curve as found in our study parallels closely that of Garrahan. In comparing

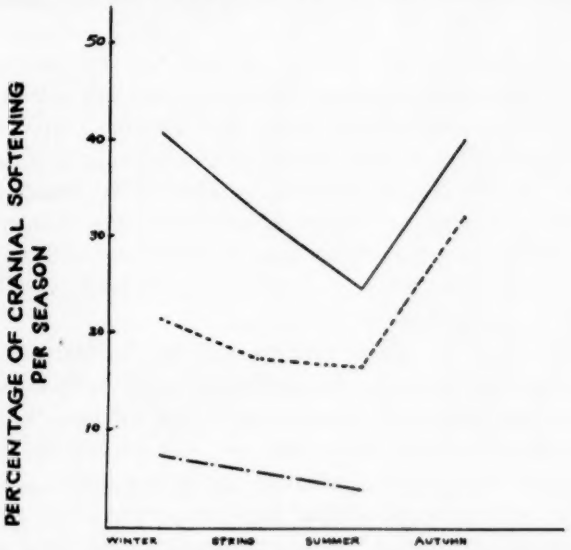

Chart 10.—Seasonal incidence of congenital cranial softening as reported by Hughes and Garrahan and in the present investigation. The solid line represents this study, the dotted line Hughes' and the line of dots and dashes Garrahan's. Values for the line representing Hughes' study were estimated from curves and for that representing Garrahan's from tables. Since the seasons in the Argentine are in reverse order from those in the United States, Garrahan's data from summer to winter are tabulated as from winter to summer.

our results with those of Hughes, a great similarity in the character of the seasonal curve is also observed. It may be noted, however, that while in our study the incidence of congenital cranial softening is practically the same in winter as in autumn and in both is considerably higher than the yearly average incidence, in Hughes's study the winter incidence not only is considerably lower than that of autumn but even falls slightly below the yearly average. Moreover, in his study, as in ours, there is a sudden and unexplained rise in the frequency of con-

genital cranial softening in the month of September. It may also be noted from table 21 that aside from the lower winter incidence of this anomaly as recorded in Hughes's data, the seasonal curve as noted in our investigation appears to undergo less fluctuation than that of the two studies with which it is compared.

In summing up, we may state that a statistically significant seasonal variation in the incidence of congenital cranial softening has been observed in the present study. This seasonal variation in incidence coincides fairly closely with the seasonal variation of the sunshine curve. It would therefore appear that we might be justified in concluding that sunshine exerts a certain influence on the prenatal development of the skull, at least with respect to the development of congenital cranial softening.

The next question which arises is whether the seasonal variation in incidence of congenital cranial softening may be directly attributed to the corresponding seasonal variation of the sunshine curve, or whether it is an indirect effect of some other related etiologic factor of this anomaly, which is per se subject to a seasonal variation. With this possibility in mind, we proceeded to determine whether there is an analogous seasonal variation in certain body measurements of the infant at birth, which were previously shown to present a statistically significant correlation with congenital cranial softening.[5]

The results may be briefly summarized by the statement that no definite seasonal variation in the birth weight or occipitofrontal head circumference was observed in our series of 800 infants. Furthermore, the seasonal incidence was determined not only for all the infant skull groups combined but also for each skull group separately. The results clearly illustrated that in all seasons the osteoporotic skulls predominate among infants of the smaller weight and head circumference groups.

In regard to crown-heel length, a slight, ill defined seasonal fluctuation was observed, which statistically was only suggestive. It may thus be readily seen that the seasonal incidence variation of congenital cranial softening not only occurs independently of the corresponding variation in length, but is even distinctly opposite from what would be expected, considering that the osteoporotic skulls tend to occur more frequently in infants of smaller length groups.

Three other tables, not presented here, were prepared, which showed the seasonal variation of birth weight, length and head circumference in the white, the Mexican and the Negro group separately. The results indicated no statistically significant variation for any of these measurements.

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5. The results of our investigation pertaining to the nature of seasonal influence on the body measurements mentioned as observed in Los Angeles will appear in a separate publication.

In order to rule out the influence of race on the seasonal incidence of osteoporosis, the seasonal distribution of each of the three racial groups was studied. It was revealed that the racial distribution throughout the year had been uniform. If anything, a slight preponderance of the Negro infants was observed in the summer, when the incidence of the osteoporotic skulls is lowest.

We may thus readily conclude that the seasonal variation of congenital cranial softening is dependent neither on the seasonal variation of birth weight, length and head circumference nor on the seasonal predominance of any racial group in our series of infants.

There are a number of studies available on the seasonal variation of birth weight and length (Marshall; Bakwin and Bakwin; Brenton; Abels; Adersen; Hansen; Li; Murray; Toverud [1933]; Faber), although there are not so many on the seasonal variation of other measurements. Opinions in regard to the seasonal variation of birth weight and length are divided. Bivings reported a seasonal variation of birth weight, which followed inversely the curve of sunshine. This he attributed entirely to the effect of ultraviolet radiation. It is of interest that the seasonal variation of birth weight as reported by Bivings coincides with the seasonal incidence variation of congenital cranial softening as found in our study.

COMPARATIVE INCIDENCE AS GIVEN BY VARIOUS AUTHORS

In studying the cause of congenital cranial softening, especially its alleged relation to rachitic manifestations, it would be of unquestionable interest, in addition to the investigation of seasonal variation, to compare the incidence of this condition as found in various localities with diverse climatic conditions. Unfortunately, as brought out previously, the lack of a uniform objective criterion of what constitutes a soft or osteoporotic skull would make such a comparison almost valueless. For the sake of completeness, however, all the available figures on the incidence of congenital cranial softening are presented in chart 11.

On the other hand, we believe that we are justified in attempting to compare our results with those of Toverud, for the following reasons: (1) a similar threefold classification of the infants' skulls into "hard," "transitional" and "soft" has been used; (2) a strong attempt was made by us, by means of a personal communication as well as by a careful study of the article on congenital osteoporosis published by Toverud in 1932, to follow as closely as possible the standards for skull classification used by this author. In a personal communication in 1937, Toverud stated that although such a classification as used in our respective studies must unfortunately be subjective, she believed our classification to be similar to that used by her. She likewise expressed

the opinion that if an error in classification was committed in our study it was in the direction of having too large a number in our "soft skull" category. A comparison of the results obtained in our respective investigations pertaining to the effect of the maternal diet during pregnancy on the development of congenital cranial softening has been presented in a previous section of this study.

The distribution of hard, transitional and soft skulls as found in Toverud's series of 200 infants and in ours of 800 is presented in table 2 and chart 11. In order to make our results still more comparable,

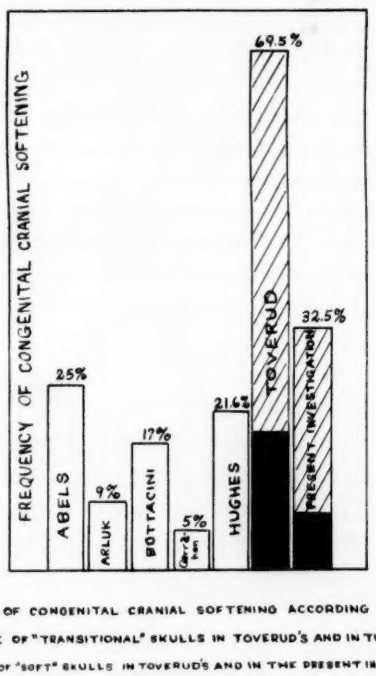

Chart 11.—Percentage of congenital cranial softening observed by various investigators compared with that observed in the present investigation. (The data on the other studies were adapted from Garrahan and Traversaro.)

our white racial category, which we believed would correspond more closely to Toverud's subjects, was alone used for comparison.

It may be readily seen from table 2 that the incidence of infants with transitional and soft skulls in Los Angeles is less than half of that in Oslo, Norway. The differences in distribution of hard, transitional and soft skulls as well as the actual distributions as found in these two localities are statistically significant (table 2). It would appear to us that these results tend to indicate further that possibly, as in the causation of rickets, the climate or, more specifically, the character of

the sunshine with respect to ultraviolet radiations may be a contributing factor in the development of congenital cranial softening.

COMMENT

An evaluation of the relative importance of the factors studied, as regards their relation to congenital cranial softening, has been based primarily on the results of the statistical analysis, i. e., on the degree of statistical significance obtained. In instances in which a definite statistical significance was not obtained, the results were still taken into consideration, providing a definite, consistent trend was present, when in addition it had been observed previously by other investigators.

We are confronted, however, with the difficulty of interpretation of the results obtained, and we are far from being prepared at the present time to explain to our satisfaction the greater part of them. For this reason only a brief discussion will be presented.

In connection with the factors pertaining directly to the infant, the highest degree of correlation was observed between, on the one hand, the anomaly under consideration and, on the other, the occipitofrontal head circumference and the birth weight. Less pronounced was the relation to the crown-heel length. From these results we may definitely conclude that congenital cranial softening shows a predilection for the smaller infants. In the light of the observation of Rosentern and Hottinger (*a*), that congenital cranial softening is met with less frequently in the premature infant, the interpretation of its predilection for smaller infants becomes difficult. Wieland's theory that congenital cranial softening is a physiologic manifestation rather than a pathologic one, which is brought about by a discoordination between the rapid growth of the brain and the calcification processes in the vertex of the skull during the last month of gestation, adds to the difficulty of the interpretation of the greater frequency of this anomaly in infants of the smaller head groups. Is congenital cranial softening a sign of skeletal immaturity, or is it perhaps, as Abels and Karplus stated, a sign of constitutional inferiority of the skeleton? We are not prepared to answer this question.

The question of cranial molding in relation to congenital cranial softening is another matter of interest which presents some difficulty in interpretation. The fact that molding occurred less frequently in the infants with congenitally soft skulls than in those with the hard may indicate either that the infants with soft skulls are subject to less molding because of the smaller size of the head in the majority, or that their skulls are more flexible and resilient and therefore return to the normal shape faster. It being known that premature infants are more subject to intracranial birth injuries partly because of the greater compressibility

of their skulls (von Haam; Holland), the question arises as to whether infants with congenitally soft skulls are perhaps also more susceptible to intracranial injury than the infants with hard skulls. We are not prepared to answer this question. We believe that the study of the frequency with which cephalhematoma occurs in infants with soft skulls as compared with those with the hard would be of definite value, and we are at present attempting to collect a larger amount of data on this subject.

It would appear to us that the absence of any degree of cranial softening in infants born by breech presentation, as observed in our study—a finding possessing statistical significance in spite of the relatively small number of infants in this group—would tend to confirm the belief expressed by Hughes and by Abels that congenital cranial softening is brought about chiefly by the pressure of the fetal head against the rigid lower uterine segment and the pelvic bones. A confirmation of the same finding in a study of a larger number of infants born by breech presentation, an investigation now going on, would in our opinion throw considerable light on this point.

The greater incidence of facial asymmetry in the infants with transitional and with soft skulls is another finding of interest which is subject to various interpretations. Because of the alleged mechanical causation of both congenital cranial softening and facial asymmetry we may conclude that the higher incidence of the latter anomaly in infants of the osteoporotic skull group represents further proof of increased intrauterine pressure effects in the case of these infants. On the other hand, the greater incidence of facial asymmetry in infants with osteoporotic skulls might be looked on as further evidence for Toverud's view, namely, that congenital cranial osteoporosis is a manifestation of a generalized osteoporotic process throughout the entire osseous system of the newborn child. In other words, it is not unlikely that the position of the infant in utero, resulting in certain pressure effects, is not the sole etiologic factor of facial asymmetry, as claimed by Parmelee, but that an osteoporosis of the facial bones which could render them more plastic and pliable to pressure is another important causative factor. The somewhat greater incidence of conically shaped chests in infants with soft skulls is likewise of interest from this standpoint.

In this connection we may mention the work of Greene on asymmetry of the head in infants and that of Hess (1931) on the so-called "flat head, soft chest syndrome." Greene pointed out that the asymmetry of the head which frequently develops in infants during the first year of life, apparently as a result of a preference shown by the infant to lie on one or the other side of the head, may result in permanent dentofacial asymmetry and even deformity. He stated the belief, although he

presented no conclusive evidence, that this condition is due to osteoporosis of the craniofacial bones in these infants at birth. Hess definitely concluded that the flat head, soft chest syndrome, which he observed in infants and older children, is not a rachitic manifestation but is due to an osteoporosis of the respective bones at birth.

Our finding of a more frequent occurrence of facial asymmetry and of conically shaped chests among infants with soft or osteoporotic skulls would appear to corroborate to some extent the theories of Hess and of Greene. Moreover, if further evidence could be presented that congenital cranial softening is a factor predisposing to the development of dentofacial deformities, it might explain why thumb sucking or improper sleeping positions in infancy appear to bring about dentofacial and orthodontic deformities in some children and not in others. In order to determine what significance congenital cranial softening, or osteoporosis, may have in respect to the development of pathologic conditions of the skeleton in the infant during the first year of life, we believe that a follow-up investigation of these and of normal control infants would have to be made from birth, not only with respect to the development of rickets and postnatal craniotabes but also with respect to the appearance of the deformities and asymmetries mentioned. Moreover, it would be of interest to observe the condition of the deciduous teeth in infants who at birth presented cranial softening, for the development of the deciduous teeth is completed during the prenatal period (Toverud [1932]; Freudenberg; and others). If an enamel hypoplasia of the deciduous teeth is a fetal disturbance in calcification analogous to the congenital vertex softening of the cranial bones, as claimed by Freudenburg, one might expect to find a certain degree of association of the two.

We believe that considerable light could also be thrown on the nature and cause of the anomaly under consideration, by a study of its incidence and mode of occurrence in twins. If it is brought about by a prenatal environmental or maternal factor, such as a lack of calcium and phosporus or of the fat-soluble vitamins of the maternal diet or an insufficient exposure to sunshine, it would be logical to expect to find not only a greater frequency of this anomaly among twins, but also a similar state of cranial calcification in the two twins of any given pair. If, on the other hand, cranial softening were to be met with in one of the twins only, it would be necessary to consider the possibility of the existence of a constitutional factor and look for an explanation of its origin to the germ plasm or perhaps look to the play of certain intrauterine pressure effects. We are at present conducting such a study.

The higher incidence of so-called minute developmental defects and other congenital anomalies in infants of the osteoporotic skull group is an interesting finding in the light of the view expressed by Sokolow and

other investigators (Bauer [*a*]; Pende) that such conditions are stigmas of degeneration. Sokolow maintained that even the minute developmental defects if multiple are indicative of a constitutional inferiority in the infant.

In regard to the evaluation of the relative importance of the maternal factors studied, it may be pointed out that only a few of these showed a statistically significant correlation with the anomaly in question. However, as has been indicated previously, the fact that the observations with respect to the maternal factors were conducted on a much smaller group of subjects than were those with respect to factors pertaining directly to the infants might be a cause for the failure to find a higher degree of significance in these results. However, a fairly high degree of correlation was noted between congenital cranial softening, on the one hand, and, on the other, the maternal exposure to sun during pregnancy, the order of birth of the infant and the maternal age when the primiparas and multiparas were considered separately.

With respect to the first of these factors it would appear that sunshine, as it is in the case of rickets, may be an etiologic factor in the development of this anomaly. The finding of a statistically significant seasonal variation in its incidence, which follows inversely the curve of sunshine, would further tend to support this inference.

In this connection it is also interesting to note the observation of some investigators (Moore and Dennis), among them Eliot and Park, that the peak for the occurrence of postnatal, or so-called rachitic, craniotabes is in winter and early spring. Since the majority of infants so affected are then 3 and 4 months old, which is the age when the postnatal craniotabes usually makes its appearance, it would seem that their months of birth coincide with the seasons when, according to our figures, the incidence of congenital cranial softening is highest. It would appear to us that this finding tends to support Hughes's view, namely, that there is a definite relation between the two types of cranial softening.

The greater occurrence of congenital cranial softening among the Negro infants of our series, a finding to be expected in view of the filtering action of the heavy pigmentation of their skin on the ultraviolet radiations, would also seem to be in accord with the inference that sunshine exerts an influence on the prenatal development or the calcification of the infant's skull. On the other hand, this racial variation in incidence, which statistically is not fully significant, probably because of the small number of infants in our Negro group, might be open to still another interpretation. Since our results have also shown that the average size of the Negro infant is less than that of the white or the Mexican, we must consider the possibility that the racial variation of this anomaly in favor of the Negro may be due to its known predominance

in smaller infants. The latter view would appear to find support in the fact that no statistically significant difference in the incidence of this anomaly was found between our much larger white and Mexican racial groups. Because of the insufficient number of infants in our Negro group, we are now trying to observe a larger number of Negro infants, in order to see whether the same results would be manifested.

The preponderance of congenital cranial softening in the first and second-born infants in contrast to those born later would seem to support the mechanical causation theory, for, as is known, the infant is subject to greater intrauterine pressures in the primipara than in the multipara (Davison; Abels and Karplus). The peculiar age distribution observed, peculiar because of the greater incidence of congenital cranial softening in offspring of younger multiparas and other primiparas, would also appear to corroborate this theory.

Both of these findings would seem to speak against the state of the calcium storage or the calcium balance of the mother as an etiologic factor of this anomaly, in the light of some available evidence that frequent pregnancies exert a depleting action on the maternal calcium storage (Rector; Dieckmann; Mull and Bill) and even on the maternal blood calcium level (Mull and Bill). Our failure to find a definite relation between the calcium and phosphorus content of the maternal diet and congenital cranial softening likewise speaks against an antepartum calcium deficiency as an etiologic factor. We are not prepared to explain our failure to confirm Toverud's results with respect to the effect of the maternal diet on the calcification of the infant's skull despite our endeavor to make our dietary standard and our criterion for skull classification as similar to hers as is possible in a clinical study of this type.

In order to provide further evidence for the theory that a deficiency in the calcium content of the maternal diet during pregnancy is the main etiologic factor of congenital cranial softening, or osteoporosis, as asserted by Toverud, we are planning in the near future to conduct a control study on a group of Mexican infants in the native Mexican environment at the level of Mexico City, to compare with the observations made on the group of Mexican infants in this study. As has been pointed out previously, the diet of the native Mexicans, even of those of the lower economic levels, in that locality seems to be adequate, if not actually high, in calcium and phosphorus (Torroella), although it is deficient in other constituents of a balanced diet. This unusual condition, unusual because the average American and European diet is generally deficient in calcium, is the result of a high intake of lime-treated corn tortilla and dry pink beans (Ramos Espinosa [1935]). Moreover, the sunshine conditions, with respect to the availability of the ultraviolet radiations, are even more favorable there than in Los Angeles, although the climatic conditions in these two localities are fairly similar. We believe that by

having the same examiner and the same racial stock of people but more favorable conditions for calcium assimilation and balance in one locality than in the other, we should have as careful a control study as is possible in a purely clinical investigation. We should then be able to draw some definite conclusions from the comparison of the incidence of this anomaly in these respective localities.

SUMMARY

The main part of this investigation consisted of studying the incidence of congenital cranial softening or osteoporosis, known variously as congenital craniotabes, as craniomalacia and as vertex softening, in 800 nonselected, full term newborn infants; also, its association with various maternal, infant and climatic factors.

A comparative study of the results of this investigation with those of other investigations previously reported was made, with special reference to the geographic distribution of congenital cranial softening.

This study differs from those the records of which are available to the authors in that race and climatic conditions as well as the effect of the maternal exposure to sunshine during pregnancy were considered as possible etiologic factors. The alleged relation of this anomaly to rickets was investigated by the observation of its frequency and severity under a type of climate such as exists in southern California, where the incidence of rickets is relatively low.

The results obtained from the statistical analysis of the data were as follows:

1. A statistically significant seasonal variation in the incidence of congenital cranial softening was observed. The variation followed inversely the curve of sunshine, being highest in winter and fall and lowest in summer and spring.

2. No congenital cranial softening was found in any of our series of 24 infants born by breech presentation.

3. A statistically suggestive racial variation was noted in the incidence of congenital cranial softening, since it was found to occur twice as frequently in the Negro infants as in either the white or the Mexican group.

4. No significant seasonal variation was observed in the infant birth weight, the crown-heel length or the occipitofrontal head circumference.

5. A statistically significant positive (or direct) correlation was shown between congenital cranial softening and the following sets of factors: in the infant, facial asymmetry and softness of the cranial sutures; in the mother, maternal age among primiparas. A statistically significant negative (or inverse) correlation was shown between congenital cranial softening and the following sets of factors: in the infant, birth weight, occipitofrontal head circumference, crown-heel length,

degree of cranial molding and the number of minute developmental defects, and other congenital anomalies; in the mother, none.

6. A statistically suggestive positive (direct) correlation was shown between congenital cranial softening and the following sets of factors: in the infant, size of the anterior fontanel, degree of separation of the cranial sutures and conically shaped chest; in the mother, calcium and phosphorus content of the maternal diet during pregnancy. A statistically suggestive negative (inverse) correlation was shown between congenital cranial softening and the following sets of factors: in the infant, order of birth; in the mother, exposure to sun during pregnancy (almost significant), maternal age in multiparas, parity i. e., higher incidence in primiparas (almost suggestive) and amount of rest and sleep during pregnancy (almost suggestive).

7. No correlation was observed between congenital cranial softening and the following sets of factors: in the infant, sex, presence or absence of cephalhematoma, presence or absence of additional fontanel, degree of tibial bowing, open or closed posterior fontanel, and presence or absence of engorgement of the breast; and in the mother, interval between births, maternal health during pregnancy (with respect to certain complications, e. g., toxemia and hyperemesis), health of the parents at the time of conception, amount of physical work done during pregnancy, type of delivery, and dental caries (almost a suggestive positive correlation).

8. In addition a statistically suggestive correlation was noted between the following sets of factors: season of birth and infant's length at birth; infant weight, length and (occipitofrontal) head circumference, on the one hand, and race on the other; infant birth weight and parity; type of diet and race.

The significance that congenital cranial softening may have in connection with the development of pathologic conditions of the osseous system during the first year of life is discussed in the light of available knowledge and theories. Apparent reasons for the controversy in regard to the present status of the subject are outlined. Problems for further investigation are presented.

CONCLUSIONS

1. There is a significant seasonal variation in the incidence of congenital cranial softening, which is inverse to the curve of sunshine.

2. The apparent relation of congenital cranial softening to lack of sunshine is further corroborated by the following observations: (*a*) that the incidence of this anomaly is lowest in infants of mothers who have reported an abundant exposure to sun during pregnancy, and (*b*) its incidence in southern California as observed by us is half that reported by Toverud in Norway.

3. Congenital cranial softening shows a definite predilection for infants of the smaller birth weight, crown-heel length and occipitofrontal head circumference groups.

4. There appears to be no significant seasonal variation in the infant birth weight, the crown-heel length or the occipitofrontal head circumference under the conditions of the present study.

5. Certain evidences for the mechanical causation theory of congenital cranial softening have been found in this study, such as the absence of this anomaly in all the infants born by breech presentation, its more frequent occurrence in the first-born and second-born infants and its predilection for offspring of older primiparas and younger multiparas.

6. The results of this study fail to confirm Toverud's finding that congenital cranial osteoporosis is caused by a deficiency in the calcifying factors, especially in calcium, of the maternal diet during pregnancy. The lack of definite evidence of a relation between congenital cranial softening in the offspring and the calcium and phosphorus content of the maternal diet might be considered as evidence that no such relation exists, at least under the conditions of this study.

7. It would appear that a deficiency in vitamin D during pregnancy, rather than in the calcium and phosphorus of the maternal diet, might be an etiologic factor of congenital cranial softening.

Dr. Ethel C. Dunham and Dr. Emil Bogen made valuable suggestions during this study; Dr. Bengt Hamilton and Dr. Mandel L. Spivek gave criticism of the paper, and Dr. J. A. Gingerelli assisted in the choice of the statistical treatment of the results.

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A STUDY OF TWO HUNDRED AND FORTY BREAST-FED AND ARTIFICIALLY FED INFANTS IN THE ST. LOUIS AREA

II. INCIDENCE OF RASHES AND GASTROINTESTINAL DISTURBANCES IN BREAST-FED INFANTS AND IN INFANTS FED ON FRESH MILK FORMULAS AND ON ACIDIFIED (LACTIC ACID) AND NONACIDIFIED EVAPORATED MILK FORMULAS

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Although the major part of this study was concerned with the antirachitic value of different types of widely used feeding formulas, much interest was felt too in other aspects of the subject, such as the incidence of diarrhea, rashes, colic and infections in the groups studied. The careful following of these groups, it was felt, might help to answer some still debatable questions concerning the relative values of acidified and nonacidified evaporated milk formulas and to establish whether any significance should be attached to the belief which is apparently held by some pediatricians that irradiation leads to increased incidence of rashes, colic and even diarrhea. Another interest at the beginning of the project was to study intensively all cases of severe diarrhea developing in any group. The details of the investigation are described in the preceding paper.

OBSERVATIONS

Gastrointestinal Disturbances.—Of 208 infants considered (the infants followed for as short a period as six months are not included here), 86 had diarrhea (table 1).

The illness in most cases was mild. Treatment consisted in giving dilute unsweetened formulas without solids until the stools became normal; the basic formula was not changed. Infants with severe illness were hospitalized. Dysentery organisms were not found in any case.

Forty-six per cent of the cases of diarrhea occurred in July, August and September. There was a lower incidence of diarrhea in the breast-fed infants than in any other group; the highest incidence was in the group receiving whole milk. The frequency of diarrhea in the group fed nonirradiated evaporated milk was slightly greater than in the group

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fed irradiated milk. Of all the infants who were fed acidified evaporated milk, 40.2 per cent had diarrhea, as compared with 44.1 per cent of the infants receiving simple evaporated milk formulas.

With regard to early feeding difficulties, such as regurgitation, colic, vomiting, constipation and irritability, there was no demonstrable difference between the infants given lactic acid and those not given lactic acid. The babies gained equally well.

TABLE 1.—*Incidence of Diarrhea in Infants Grouped According to Type of Feeding*

Feeding	Subjects	Diarrheas		Severity			Quarter of Year			
		Number	%	1	2	3	1	2	3	4
Breast	37	6	16.2	4	2	0	2	0	4	0
N.I.E.	30	16	53.3	11	4	1	1	6	6	3
N.I.E.-L.A.	24	10	41.7	7	3	0	2	2	4	2
E.-135	26	11	42.3	6	3	2	3	3	2	3
E.-135-L.A.	27	9	33.3	8	1	0	1	1	5	2
E.-200	30	11	36.7	9	2	0	1	1	9	0
E.-200-L.A.	21	10	47.5	5	5	0	2	1	5	2
W.M.-200-A.	25	13	52.0	11	2	0	3	1	5	4
Total	208	86	....	61	22	3	15	15	40	16
Average	...	..	41.2							

N.I.E. = nonirradiated evaporated milk.
N.I.E.-L.A. = nonirradiated evaporated milk with 0.5 per cent lactic acid.
E.-135 = irradiated evaporated milk, 135 U. S. P. units of vitamin D to the reconstructed quart.
E.-200 = 200 unit irradiated evaporated milk.
E.-200-L.A. = 200 unit irradiated evaporated milk with 0.5 per cent lactic acid.
W.M.-200-A. = 200 unit irradiated whole milk.

TABLE 2.—*Rashes in Infants Grouped According to Type of Feeding*

Feeding	Subjects	Rash		Severity		Other Allergy	Family Allergy	Quarter of Year			
		Number	%	Slight	Moderate			1	2	3	4
Breast	37	3	9.3	3	0	0	1	2	1	0	0
N.I.E.	42	5	11.9	4	1	1	2	3	0	0	2
E.-135	61	14	23.0	10	4	2	4	8	4	1	1
E.-200	51	7	12.9	7	0	1	2	3	2	1	1
W.M.-200	49	9	18.3	5	4	1	3	4	2	0	3
Total	240	38	15.8	29	9	5	12	20	9	2	7

Rashes.—Table 2 shows the occurrence of rashes in the entire 240 subjects. The rashes considered were the dry, papular, scaly, sometimes indurated variety, which suggest or develop into eczema. They appeared most frequently in January, February and March, and all cleared up without change of milk. In 29 of 38 infants the rashes were mild; in 9, moderate; in none, severe. There were fewer rashes in the breast-fed than in any other group; in the group fed irradiated milks there was a slightly higher percentage of rashes than in that fed

nonirradiated milk. A family history of allergy was present in 12 cases. The treatment consisted in the use of an elimination diet (usually it was necessary to omit only wheat and egg) and tar ointment.

COMMENT

The superiority of breast feeding with regard to the incidence of diarrhea is clearly seen in this study; similar results were reported by Williams and Kastler.[1] Kositza [2] showed that diarrhea is less common in babies fed evaporated milk than in those fed whole milk; this is confirmed in the present work.

Lactic acid was used in about half of the evaporated milk formulas. There is a small difference in favor of the group fed lactic acid as regards diarrhea, but this difference is not great enough to be statistically significant. In 1929 Brennemann [3] reported an extensive study in which he could find no difference in the welfare of infants fed a simple evaporated milk formula and those fed a lactic acid–evaporated milk formula. The present study has not demonstrated any advantage in the use of lactic acid. It should be noted, however, that the summer of 1938, during which this investigation was carried on, was one which produced practically no diarrrhea of the severe variety in the St. Louis area.

Breast-fed infants had the least amount of eczema in our series; Grulee and Sanford [4] reported a similar finding. Experiments carried out by Hogan and Richardson [5] on rats showed that a dermatitis developed when the vitamin B food carrier had been exposed to ultraviolet radiation; this was attributed to the destruction of part of the vitamin B complex by ultraviolet radiation. The question arose as to whether the feeding of irradiated milk would, for the same reason, bring about more rashes than that of nonirradiated milk. There was, it is true, a slightly lower percentage of rashes in the infants fed nonirradiated as compared with those fed irradiated milk. However, since all the infants in whom rashes appeared numbered only 38, and since all the rashes cleared up without change of milk, one cannot conclude that the higher incidence of rashes is evidence against irradiated milk. Further observations in a larger series would be interesting.

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1. Williams, C. T., and Kastler, A. O.: J. Pediat. **4**:454, 1934.
2. Kositza, L.: J. Pediat. **1**:456, 1932.
3. Brennemann, J.: Curd and Buffer in Infant Feeding, J. A. M. A. **92**:364 (Feb. 2) 1929.
4. Grulee, C. G., and Sanford, H. N.: J. Pediat. **9**:223, 1936.
5. Hogan, A. G., and Richardson, L. R.: J. Nutrition **8**:385, 1934.

SUMMARY

Two hundred and forty infants were studied over a period of twenty months with respect to gastrointestinal disturbances and rashes accompanying different feedings. The following observations were made:

1. Breast-fed infants had the lowest incidence of both diarrhea and rash.

2. No advantage was seen in the use of lactic acid formulas as regards early feeding difficulties, such as colic, constipation or regurgitation.

3. Infants fed whole milk were more liable to diarrhea than those fed evaporated milk.

4. Diarrhea was slightly more common in the group receiving simple evaporated milk than in that receiving a lactic acid–evaporated milk formula. This difference was too small to be significant.

5. Infants fed irradiated milk had a somewhat higher incidence of rashes than those fed nonirradiated milk.

6. All rashes cleared up without change of milk.

FACTORS INFLUENCING APPEARANCE OF CENTERS OF OSSIFICATION DURING EARLY CHILDHOOD

II. A COMPARATIVE STUDY OF DEGREE OF EPIPHYSIAL OSSIFICATION IN INFANCY UNDER VARYING CONDITIONS OF DIET AND HEALTH

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In 1939 standard tables showing the time and order of appearance of centers of ossification between birth and the age of 5 years were published,[1] and in the same year a study was presented showing how the orderly progress of ossification in individual children may be modified by illness.[2] It was pointed out that the epiphysial rating was a sensitive indicator of the physical health of the child.

This paper presents the results of a group study of the effect on epiphysial ossification of disturbances of health during the first year of life and also of the effect of certain variations in diet during the same period. Epiphysial ossification is not to be confused with skeletal maturity as defined elsewhere.[3]

MATERIAL

From the children enrolled in the research series of the Associated Foundations, 25 white boys and 25 white girls were selected who had been entirely or largely breast fed for three months or more. These children were examined routinely at 3 months, 6 months, 9 months and 12 months of age. At each examination roentgenograms were made of the left shoulder, elbow, hand and wrist, hip, knee, foot and ankle and of the lateral aspect of the skull; a comprehensive set of anthropometric measurements was compiled; a record of diet and health was made, and psychologic tests, Dr. L. Dewey Anderson's modifications of Gesell's schedule of infant behavior, were conducted. No child had any prolonged or severe illness or any serious accident, and all the children were certified by the attending pediatrician to be free of any gross mental or physical defect. Every

From the Brush Foundation and Department of Anatomy, Western Reserve University.

1. Francis, C. C.; Werle, P. P., and Behm, A.: Appearance of Centers of Ossification from Birth to Five Years, Am. J. Phys. Anthropol. **24**:273-299, 1939.

2. Francis, C. C.: Factors Influencing Appearance of Centers of Ossification During Early Childhood, Am. J. Dis. Child. **57**:817-830 (April) 1939.

3. Todd, T. W.: Atlas of Skeletal Maturation: I. The Hand, St. Louis, C. V. Mosby Company, 1938. Francis, Werle and Behm.[1] Francis.[2]

child from an early age received vitamin supplements, usually cod liver oil, orange juice and a cereal containing vitamin B. A few received supplemental mineral at some time during the first year, but the quantity was small and was given for a short time. The supplemental mineral was usually dicalcium phosphate ($CaHPO_4$). Children of this type, the breast fed, have been referred to as group 1.

A similar group of 50 children, group 2, consisting of 25 white boys and 25 white girls, were selected, who did not receive any breast milk or who received so small a ration of maternal milk that it could not be regarded as supplying a major portion of the diet. These children received cod liver oil and orange juice from an early age, and a larger proportion of these than of the breast-fed babies were given supplemental mineral. Furthermore, mineral was given for longer periods during the first year to almost every one of these children. The fact that the second group of children received a diet richer in mineral is significant and will be mentioned later. Children in this group also received, in general, larger doses of vitamin D.

A third group of 25 boys and 25 girls were collected who showed evidence during the first year of some difficulty in gastrointestinal adjustment. The evidences of maladjustment were varying degrees of eczema and in 5 children definite pylorospasm. The condition in each child was recognized early, and every effort was made by the attending physician to minimize the difficulty. Only 5 of the babies of this group were entirely breast fed to the age of 3 months, and they displayed eczema later when the diet was supplemented with cow's milk. All the others gave evidence of sensitivity before that age, and many had only minor manifestations after that age. Most were completely weaned by the time they were 3 months old, nearly all received supplemental feedings from birth and 8 did not receive any breast milk. About half received some supplemental mineral during the first year, and vitamins were given early. When orange juice caused eczema, some other form of vitamin C was substituted.

Among the cadavers given to the department of anatomy, there were 5 female and 8 male children of 3 months of age, 4 female and 6 male children of 6 months, 3 female children and 1 male child of 9 months and 1 female child and 5 male children of 12 months. Roentgenograms and anthropometric measurements of these 33 dead children, considered as group 4, were included in the study to show the severe retardation produced by serious illness or prolonged malnutrition. Sixteen of these children were white and 17 negro, whereas all the living children were white.

ANALYSIS OF DATA

In assembling the data it seemed best to confine this study to six measurements: two of bulk, the weight in pounds and ounces and the recumbent length in millimeters; two of ossification, the epiphysial rating in months and the number of epiphyses ossified at the end of each age interval; one of skeletal maturity in months, and one of psychomotor progress in months.

As was pointed out in the previous paper, in estimating the age equivalent of each aspect of development, standards have been used which were calculated from the children enrolled in the present series; therefore, each child is compared with other Cleveland children of superior physical and economic status.

The epiphysial ratings were obtained by assessing the roentgenograms of each child according to the standard tables published by Werle and me in 1939.[1] Ratings of skeletal maturity were made by comparing the roentgenograms with

standard films of maturation; those of the hand have already been published by Dr. T. Wingate Todd.[3] Standard films for the foot, elbow, knee, hip and shoulder have been prepared and have been in use in this laboratory for five years. The standards for the foot are being assembled in the form of an atlas at the present time.

TABLE 1.—*Results of Examination of the Four Groups of Boys*

Group	Age, Mo.	Weight Lb.	Weight Oz.	Length, Mm.	Skeletal Maturity, Mo.	Epiphysial Rating, Mo.	Number of Centers Ossified	Psychomotor Age, Mo.
1	3	14	1	603.36	2.94	2.00	8.68	3.00
	6	18	7	667.24	6.03	3.80	11.36	6.31
	9	21	10	718.40	9.24	6.76	13.40	9.44
	12	23	15	758.80	12.19	10.84	17.24	12.34
2	3	14	4	610.04	2.91	2.32	9.04	3.13
	6	18	13	673.04	6.08	4.64	12.24	5.88
	9	22	1	722.44	9.63	7.16	14.48	9.37
	12	24	3	766.00	13.12	11.08	18.44	11.82
3	3	13	14	606.80	2.94	1.92	8.28	3.02
	6	18	1	671.88	5.79	4.00	11.44	5.86
	9	20	15	717.24	8.81	6.64	13.68	8.92
	12	23		757.32	11.78	8.88	16.16	11.76
4	3	.....		567.50	1.66	1.62	7.00	.....
	6	.....		632.33	3.50	2.33	9.50	.....
	9	.....		588.00	3.50	2.00	9.00	.....
	12	.....		681.90	7.80	3.60	11.40	.....

TABLE 2.—*Results of Examination of the Four Groups of Girls*

Group	Age, Mo.	Weight Lb.	Weight Oz.	Length, Mm.	Skeletal Maturity, Mo.	Epiphysial Rating, Mo.	Number of Centers Ossified	Psychomotor Rating, Mo.
1	3	12	13	592.40	2.90	2.08	8.80	3.07
	6	16	13	655.92	5.91	4.68	13.20	6.45
	9	19	10	703.96	9.28	7.84	19.36	9.38
	12	21	8	745.00	12.27	11.56	27.12	12.18
2	3	12	10	587.68	2.87	2.56	9.48	2.93
	6	16	11	654.76	5.92	5.40	13.36	5.94
	9	19	2	701.76	9.20	9.60	20.92	8.89
	12	21	3	738.60	12.38	12.24	29.76	11.83
3	3	12	11	598.71	2.86	2.88	10.21	3.13
	6	16	7	653.08	5.84	5.12	14.20	6.03
	9	19	1	698.60	9.01	8.12	19.08	9.14
	12	20	15	741.16	12.03	10.48	24.24	11.75
4	3	.....		564.00	1.60	2.20	8.00	.....
	6	.....		638.50	4.50	3.25	11.50	.....
	9	.....		600.00	3.67	5.00	12.00	.....
	12	.....		720.00	9.00	7.00	12.00	.....

RESULTS

Table 1 summarizes the findings for male children and table 2 for female. Since the weight of the dead is greatly altered by dehydration it is not included, and of course there are no psychomotor ratings for group 4.

In weight the breast-fed (group 1) and the non-breast-fed (group 2) boys showed practically identical progress, the latter being a few ounces

heavier at each age. The boys of group 3 were almost as heavy at 3 months as those in the first two groups but were usually lighter at subsequent examinations. The three groups of girls showed similar progress, and those of group 3 were slightly lighter at 12 months. There was a tendency for the babies of each sex having some feeding difficulty (group 3) to gain weight more slowly than the other babies, and this deviation became more pronounced toward the end of the first year.

In recumbent length the three groups of living babies of each sex showed no significant variation. The dead babies were shorter, for severe illnesses which ultimately resulted in death did retard growth in length.

In skeletal maturity the boys of group 3 appeared slightly retarded at the examinations made at the ages of 6, 9 and 12 months, and the girls of group 3, though not below average, were nevertheless slightly less mature than those of groups 1 and 2. The dead babies showed definite retardation for each age group. Only 8 of the entire 33 dead babies showed no retardation, and only 1 had a maturity rating in advance of the chronologic age.

The epiphysial rating of the boys was highest among those in group 2, and the rating for those in group 3 fell farther behind at successive examinations, so that there was a marked divergence by the age of 12 months, most of the advance in the first two groups being made between the ages of 9 and 12 months. Among the girls, those in group 3 had the highest epiphysial rating at the age of 3 months, but by the age of 12 months they had fallen definitely behind the first two groups. By the age of 9 months the non-breast-fed girls had forged ahead, and at 1 year of age the girls of group 1 were well ahead of those of group 3. Among the cadavers, the epiphysial rating was much behind that of the groups of living children except in the case of girls of 3 months, the rating of this group being slightly in advance of that for group 1 but below that for groups 2 and 3. The retardation at older ages became increasingly marked. In none of the dead babies was the epiphysial rating in advance of the chronologic age.

The boys of group 2 had, as a rule, one more center of ossification at each examination than did the boys of group 1. Boys of group 3 did not fall materially behind those of group 1 until the age of 12 months, when they averaged one center less. The girls of group 3 started out with a slight advantage in the number of epiphyses ossified at 3 months; they maintained this advantage at 6 months but fell behind at 9 months and still farther behind at 1 year. Like the boys, the non-breast-fed girls showed more epiphyses ossified at 9 months and at 12 months than did the breast-fed girls. In number of epiphyses ossified, the dead boys of each age group were definitely behind any of the

groups of living boys. The dead girls at 3 months had nearly the same number of ossified epiphyses as those of group 1 and somewhat less than those of groups 2 and 3, but in later age groups they fell increasingly far behind. Attention is drawn to the fact that these female cadavers did not maintain the usual advance over boys in the number of epiphyses ossified, the average number for girls at 12 months being only 1 more than that for boys; whereas in the living subjects at 12 months the breast-fed girls had ten more, the non-breast-fed girls eleven more and the girls of group 3 eight more epiphyses ossified than did the respective groups of boys.

In psychomotor progress the various groups showed little variation, but on the whole the breast-fed babies, both boys and girls, were slightly in advance of the babies of the other two groups and the babies of group 3 were slightly behind. However, the differences are too slight and too variable to be significant.

COMMENT

In the standards of epiphysial ossification the centers are arranged in sheaves according to the order of appearance on the basis of age. Epiphysial rating is based on the most advanced center present, even though certain centers which should have ossified earlier may occasionally be entirely cartilaginous. Nevertheless the epiphysial rating is closely correlated to the number of epiphyses ossified, and statements made concerning one group of data must necessarily apply to the other.

In the data presented, epiphysial ossification is the objective finding which shows the most definite tendency to be laggard. All the living children were under the care of pediatricians; therefore, signs of difficulties were recognized early and competent measures taken to minimize the effect. Those children who had the most severe difficulties in adjustment were naturally the ones who at 12 months still showed the greatest retardation in epiphysial ossification. For example, 3 of the boys who had early and rather severe eczema had at 12 months an epiphysial rating of but 3 months. In every instance clinical evidence of gastrointestinal sensitivity at the end of the first year of life was limited to an occasional outbreak of mild eczema. No child at any time was in a dangerous condition, and no child had any prolonged, serious complications.

In these children competent and timely pediatric supervision minimized the handicap. Growth in length was maintained, gain in weight was only slightly below that of the other groups and there was no significant delay in psychomotor progress. By the age of 12 months it was only in epiphysial ossification that objective evidence was found of early difficulty, and the degree of retardation was proportional to the severity of the manifestations.

The data show that in children otherwise healthy epiphysial ossification may be influenced by the amount of mineral available in the diet. Many of the non-breast-fed children were given supplemental mineral in some form, whereas only a few of the breast-fed babies received any extra mineral. Furthermore, human milk is not rich in mineral. There is also some evidence in the dietary records that the non-breast-fed babies were given larger amounts of vitamin D. In the light of other studies in progress the advance in epiphysial rating of the non-breast-fed babies at 9 months and 12 months may be accounted for by the larger supply of mineral available in the diet and perhaps also by a larger quantity of vitamin D.

MacNair and Roberts,[4] in a recent study of the effect of a milk supplement on the physical status of children in an institution, found that the addition of a pint (473 cc.) of milk per day to the diet caused greater progress in development of the bones of the wrist as indicated by the Carter ossification ratio. The regular institutional diet lacked a number of dietary essentials. The addition of a pint of milk, although it did not make the diet perfect, did add enough constituents to the diet to make a considerable difference in skeletal development.

Many of the babies of group 3 were given supplemental mineral, and all received large quantities of vitamin D. In these children the difficulty was one of utilization of material available in the diet and not one of suboptimal diet. The early and continued reenforcement of the diet with mineral and vitamins seems to have prevented more marked retardation in epiphysial ossification in many children.

The data on the dead children clearly show the decided delay in epiphysial ossification resulting from severe illness. Standards of epiphysial ossification based on studies of cadavers or diseased children do not register an accurate pattern of healthy progress. It is fully realized that the number of cadavers in this series is not great, but their ratings are so far behind those of the living children that the findings are significant.

The failure of the number of centers ossified in the female cadavers to remain in advance of that in the male suggests that the precocity seen in living female babies is not due to sex alone. This phase of the problem requires further study.

SUMMARY

Epiphysial ossification is a more delicate objective indicator of constitutional health than is progress in height or weight.

4. MacNair, V., and Roberts, L. J.: Effect of a Milk Supplement on the Physical Status of Institutional Children: II. Ossification of the Bones of the Wrist, Am. J. Dis. Child. **56**:494-509 (Sept.) 1938.

Gastrointestinal sensitivity in infancy, even when so well controlled that there is no retardation of growth in length, nevertheless tends to retard epiphysial ossification.

In healthy children the degree of epiphysial ossification is influenced by the amount of mineral available in the diet.

Severe or prolonged illness holds back general progress, but epiphysial ossification shows the greatest retardation.

The advance in precocity of the female child over the male child in epiphysial ossification disappears in severe prolonged illness.

ENURESIS

A STUDY OF CAUSES, TYPES AND THERAPEUTIC RESULTS

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This study is an analysis of findings in 100 representative children observed in our enuresis clinic. It is an effort to provide successful diagnostic and therapeutic aids. The child who has reached the age of 3 years and has then or at any age thereafter urinary incontinence when asleep, either diurnal or nocturnal or both, we consider to have enuresis. The symptom is often of serious import, and the attitude of assuming that the child "will outgrow it" and that the enuresis needs no treatment if cajolery or threats fail is unjustifiable. Such an attitude is "indicative of superficial understanding of such a complex, deep-rooted instinctually related symptom." [1] The investigation has included the securing of histories, physical and roentgenologic examinations, studies of vesical and neuromuscular function and various degrees of child analysis.

The following remarks are concerned with: (1) a résumé of the psychosomatic significance and of the types of enuresis, known facts about bladder function, therapeutic methods and results as reported in recent literature; (2) a consideration of the results of examinations of our patients, our clinical classification based on causative factors and the results of treatment.

It is natural that a symptom having somatic and psychic significance would have many explanations as to cause. The literature is voluminous and was well reviewed up to 1930 by Anderson.[2] The causes may be conveniently grouped as organic and psychogenic. The organic causes can best be divided into local vesical and general physical factors, and neurologic factors of the organic type. Trousseau [3] described enuresis

From the Department of Urology, Children's Mercy Hospital.

1. Michaels, J. J., and Goodman, S. E.: Incidence of Enuresis and Age of Cessation in One Hundred Delinquents and One Hundred Sibling Controls, Am. J. Orthopsychiat. **8**:460-465 (July) 1938.

2. Anderson, F. N.: Psychiatric Aspects of Enuresis, Am. J. Dis. Child. **40**: 591-618 (Sept.); 818-843 (Oct.) 1930.

3. Trousseau, A.: Lectures on Clinical Medicine Delivered at the Hôtel Dieu, Paris, translated by J. R. Cormack and P. V. Bazire, Philadelphia, Lindsay & Blakiston, 1873, vol. 2, p. 297.

as a clinical entity and considered it an expression of an irritable bladder. Fuchs's [4] studies on soldiers, reported in the first comprehensive treatise on enuresis, caused him to conclude that a sphincteral weakness in many and spina bifida in others was the cause. Others concluded that a thickened musculature of the bladder prevented adequate distention [5] or that spasmophilia [6] associated with increased galvanic response was a cause. Campbell [7] studied 259 patients from under 5 to 15 years of age in whom medical treatment failed and found organic disease in 50 per cent; 25 per cent were cured and 50 per cent were improved under urologic or surgical treatment. He concluded that if no uropathy were found the vesical control would eventually become normal. As to general physical factors, allergy,[8] syphilis [9] and fatigue [10] have been considered as causes. On the other hand, Christoffel [11] proved experimentally that actively playing children had less enuresis or none when fatigued.

Among the neurologic causes, spina bifida was reported a factor by Hamburger,[12] Fuchs,[4] Peritz (35 per cent in 20 cases), Arnesen (53.5 per cent), and Kohler (60 per cent).[2] Mertz [13] concluded that spina bifida is seldom a cause of dysuria except in severe cases and that surgical procedure is warranted only in older children with severe lesions after puberty is reached. Of 6 patients operated on, 2 were definitely relieved, 2 only slightly and 2 not at all. Karlin [14] presented an interesting study to show that, of children with no urinary complaints at all and considered normal, 54 per cent had spina bifida occulta, and that, of

4. Fuchs, A.: Concerning the Clinical Proof of Congenital Defects in Different Spine Levels (Myelodysplasia), Wien. med. Wchnschr. **59**:2141-2145, 1909.

5. (*a*) Feer, E.: The Management of Enuresis, Jahrb. f. Kinderh. **139**:38-43 (June) 1933. (*b*) Sturniman, A.: Das erste Erleben des Kindes, Frauenfeld, Huber & Co., 1933.

6. Macciotta, G.: Spasmophilia Forms of Enuresis in Children, Pediatria **38**: 1145-1157 (Nov. 1) 1930.

7. Campbell, M. F.: Enuresis: Its Urological Aspects, J. Urol. **28**:255-270 (Sept.) 1932.

8. Bray, G. W.: The Allergic Child, Brit. J. Child. Dis. **29**:1-8 (Jan.-March) 1932.

9. Pinard, M.: Etiology of Enuresis, Paris méd. **1**:185-197 (March 3) 1934.

10. Mohr, J. G., and Waterhouse, E. H.: Enuresis in Children, Am. J. Dis. Child. **37**:1135-1145 (June) 1929.

11. Christoffel, H.: On the Biology of Enuresis, Ztschr. f. Kinderpsychiat. **1**: 49 (June); 76 (Aug.); 105 (Oct.) 1934.

12. Hamburger, A.: Psychopathologie des Kindesalters, Berlin, Julius Springer, 1926.

13. Mertz, H. O.: Relation of Spina Bifida Occulta to Neuromuscular Dysfunction of the Urinary Tract, J. Urol. **29**:521-524 (May) 1933.

14. Karlin, J. W.: Incidence of Spina Bifida Occulta in Children With and Without Enuresis, Am. J. Dis. Child. **49**:125-134 (Jan.) 1935.

25 patients with enuresis, 84 per cent had moderate to severe degrees of spina bifida occulta. Mandel [15] quoted Legneu, of the Necker Clinic in Paris, as saying that laminectomy had been employed there for some time in the treatment of spina bifida in children with enuresis, without good results, although a high incidence of spina bifida was seen in incontinent children, and that laminectomy should not be done in children of 6 to 8 years unless a severe spinal deformity was present. Langworthy and Dees [16] studied with newer cystometrographic technic the responses of bladders in cases of spina bifida and found that the bladder and sphincter responses show varying degrees of involvement of the sacral roots, motor, sensory or both, and the results simulate those of earlier studies on controlled root sections in experimental animals.[17] Other neurologic causes include: hypertonicity of the detrusor muscle due to overstimulation by the *nerve érigente* as demonstrated by fluctuations of the filled bladder registered on a manometer [18]; heightened threshold of sensory stimuli, because of which imperative urination cannot be reflexively controlled [19]; defective cerebral control over the bladder reflex [20]; inadequately trained conditioned reflex,[21] and impairment of the deep sensation pathway in the bladder.[22]

The literature interpreting enuresis as a psychologic problem is too voluminous to permit mention of more than a few contributions. Freud [23] early stated that nocturnal enuresis is a pollution unless associated with epilepsy, and numerous authors agree with this idea of a urethral masturbatory equivalent. Etiologically, enuresis has been considered as an expression of: a fear of the opposite sex [24]; a disorganized

15. Mandel, L.: On Enuresis, Brit. J. Child. Dis. **28**:1-13 (Jan.-March) 1931.

16. Langworthy, O. R., and Dees, J. E.: Bladder Disturbances in Spina Bifida, J. Urol. **35**:213-225 (Feb.) 1936.

17. Dees, J. E., and Langworthy, O. R.: Experimental Studies of Bladder Disturbances Analogous to Those of Tabes Dorsalis, J. Urol. **34**:359-371 (Nov.) 1935.

18. Schwarz, O.: Experiments on Analysis of Enuresis Following Cold, Wien. klin. Wchnschr. **28**:1057-1068 (Sept. 30) 1915.

19. Weitz, W., and Götz, O.: On the Pathogenesis of Enuresis, Med. Klin. **14**: 729-732, 1918.

20. Bleyer, A.: A Clinical Study of Enuresis, Am. J. Dis. Child. **36**:989-997 (Nov.) 1928.

21. (*a*) Mowrer, O. H., and Mowrer, W. M.: Enuresis: A Method for Its Study and Treatment, Am. J. Orthopsychiat. **8**:436-459 (July) 1938. (*b*) Schacter, M.: Pathogenesis of Enuresis, Jahrb. f. Kinderh. **140**:234-237, 1933.

22. Ederer, S., and von Lederer, E.: On the Pathogenesis of Enuresis, Jahrb. f. Kinderh. **138**:21-30, 1933.

23. Freud, S.: Three Contributions to the Theory of Sex, translated by A. A. Brill, ed. 2, New York, Nervous and Mental Disease Publishing Company, 1916; ed. 4, 1930.

24. Gerard, M. W.: Enuresis: A Study in Etiology, Am. J. Orthopsychiat. **9**:48-59 (Jan.) 1939.

attempt of the child to get along well [25]; poor training [10]; a conduct disorder [26]; deficient inhibitory tendencies; a weak ego; a psychopathic personality [27]; a wish for attention associated with feelings of inadequacy and fear [28]; a desire to return to babyhood and the diaper stage [29]; a conflict of wishes and indecision.[30] Sometimes it has been considered a hysterical manifestation whereby deep seated anxieties are converted into a physical dysfunction.[21a] We agree with the excellent summary of these views by Feer [5a] and Gerard.[24]

Concerning the mentality of enuretic patients, it is common knowledge that those met in private practice are of average or above average ability, to a large extent, whereas those met in institutional and clinical practice [31] are often below average in intelligence. As for the hereditary factor, Hubert [32] found that 40 per cent of his patients had parents with a history of enuresis, and Addis [31a] reported 26.6 per cent. Frary [33] made an exhaustive genetic study to show that enuresis involves a hereditary rather than an environmental or physical factor and concluded that the hypothesis that enuresis is a hereditary trait "determined by a single recessive gene substitution" is correct and proved by biometric formulas.

Various classifications have been given, and the most useful recognize no single factor as a cause but attempt an inclusive grouping. Mandel [15] considered the following causative and therapeutic grouping of his patients satisfactory: (1) those with organic disease or irritant stimulation of the bladder, (2) those with neuropathic instability, (3) those with psychopathic disturbances, (4) those with endocrine dyscrasias and (5) those who were debilitated. Fraser [34] concluded that enuresis is

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25. Beverly, B. I.: Incontinence in Children, J. Pediat. **2**:718-725 (June) 1933.

26. Hamill, R. C.: Enuresis, J. A. M. A. **93**:254-257 (July 27) 1929.

27. Michaels, J. J., and Goodman, S. E.: Incidence of Enuresis in and Age of Cessation in One Thousand Neuropsychiatric Patients, Am. J. Orthopsychiat. **9**:59-72 (Jan.) 1939.

28. Adler, A.; Ellinger, P., and Furth, O.: Resorption und Exkretion, in Bethe, A.; von Bergmann, G., and others: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1929, vol. 4.

29. Bandomin, C.: A Study of Bedwetting, Ztschr. f. psychoanal. Pädiat. **3**: 29-38, 1928.

30. Esersky, J. M.; Plotitscher, A. I., and Furmanow, A. M.: Causes and Treatment of Nocturnal Enuresis in Children, Ztschr. f. Kinderforsch. **38**:233-255 (March 12) 1931.

31. (*a*) Addis, R. S.; Miller, R., and Winnicott, D. W.: Discussion on Enuresis, Proc. Roy. Soc. Med. **29**:1515-1525 (Sept.) 1936. (*b*) Anderson.[2]

32. Hubert, W. H. de B.: Aetiology of Nocturnal Enuresis, Lancet **1**:1281-1283 (June 17) 1933.

33. Frary, L. G.: Enuresis: A Genetic Study, Am. J. Dis. Child. **49**:557-578 (March) 1935.

34. Fraser, J.: Some Disturbances of Micturition in Childhood, Clin. J. **62**: 221-229 (June) 1933.

either of the obstructive type, which includes that caused by uropathy (e. g., valves, folds, stricture) and that due to neuromuscular disharmony, or of the irritable type, which includes emotional frequency and involuntary discharge due to local irritation of perineal structures of similar embryologic development.

The fundamentals of bladder physiology need to be understood by those treating enuresis. Studies by anatomic,[35] pharmacologic,[36] roentgenologic [37] and cystometric methods [38] have established clear conceptions of vesical function. The bladder is a hollow organ for the storage and evacuation of urine, having a nicely balanced control mechanism. Any irregularities of a psychologic nature influence the bladder, as is commonly known, so that frequency and even loss of sphincter tone may be produced in an otherwise normal person if the emotional stimulus is strong enough. In answering the question of how the bladder mechanism, which is largely automatic, can also be subjugated to the control of the will, we shall find the cause and more accurate ideas for the treatment of enuresis.

Micturition in the infant is a purely reflex act, and until sensations develop he is unaware of a full bladder. With growth, conditioned reflexes for urinary control may be developed and subjugated to the control of the will. The development and continued function of this control has not only an individual but a distinct social significance.

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35. (*a*) Elliott, T. R.: The Innervation of the Bladder and Urethra, J. Physiol. **35**:367-445, 1906-1907. (*b*) Langley, G. N., and Anderson, H. K.: Innervation of the Bladder, ibid. **19**:73-78, 1895. (*c*) Wesson, M. B.: Anatomical, Embryological and Physiological Studies of Trigone and Neck of the Bladder, J. Urol. **4**:279-301 (June) 1920.

36. Edmunds, C. W., and Roth, G. B.: Point of Attack of Certain Drugs Acting on the Periphery of Bladder Control, J. Pharmacol. & Exper. Therap. **15**: 189-199, 1920.

37. (*a*) Ortman, K. K., and Christiansen, H.: Roentgenologic Studies of Male Urethra and Vesical Sphincter and Mechanism of Micturition Under Normal and Pathologic Conditions, Acta radiol. **15**:258-283, 1934. (*b*) Stevens, W. E.: Some Observations on Female Urology with Special Reference to Ectopic Kidneys and Urethrography, J. Urol. **35**:241-253 (Feb.) 1936. (*c*) Van Duzen, R. E.: Neurogenic Disturbances of Vesical Function, ibid. **37**:156-165 (Jan.) 1937. (*d*) Blum, V.; Fischer, F., and Hyrntschak, T.: Cystoradioscopy, Wien. klin. Wchnschr. **33**: 677-680, 1920.

38. (*a*) Mosso, A., and Pellacani, P.: The Functions of the Bladder, Arch. ital. de biol. **1**:97 and 291, 1882. (*b*) Denny-Brown, D., and Robertson, E. G.: On the Physiology of Micturition, Brain **56**:149-190 (July) 1933. (*c*) Amberg, S.: Comparison of Impulse to Urinate to Bladder Contraction in Enuresis, Ztschr. f. Kinderh. **38**:169-181, 1924. (*d*) Langworthy, O. R.; Reeves, D. L., and Tauber, E. S.: Autonomic Control of the Urinary Bladder, Brain **57**:266-290 (Oct.) 1934. (*e*) Rose, D. K.: Various Systometrograms and Their Interpretation: Study of Preoperative and Postoperative Incontinence in Male, J. Urol. **27**:207-227 (Feb.) 1932. (*f*) Dees and Langworthy.[17]

"Education to cleanliness becomes a prototype for the future restrictions of instinctual life. Imposing inhibition on sphincters is the first decisive step toward the adjustment to the outside world, an inhibitory agency within its own personality." [39] The voluntary control over the bladder has been experimentally determined and is largely one of inhibition,[40] although there is evidence that some slight voluntary emptying control may be exerted.[28] Thus a person's voluntary control is not exercised until the desire to void occurs, and until conditions for voiding are convenient inhibition is manifested entirely through willed effort. The pathways are by way of the parasympathetic nerves. During sleep in the normal person this inhibitory effect is maintained by the unconscious mind and is carried over into the conscious or waking state at convenience; otherwise, relaxation of the vesical sphincters and expulsion of the urine occur, which is enuresis. We believe the entire success of treating enuresis consists in developing in the patient this inhibitory control. It may be developed through neuromuscular vesical education, psychiatric methods and correction when possible of local genitourinary and neurogenic pathologic conditions. Usually, some defect in one of these fields is a predominating cause.

A knowledge of vesical physiology is necessary in order to work out clinically one of the useful methods of diagnosis, namely, cystometrography. The fundamental researches and observations of Rehfisch, Elliott, Young, Sherington, Adler, Barrington and others have been summarized by Learmonth.[41] Recent studies by Denny-Brown and Robertson, Langworthy, Rose and others have translated many of the laboratory findings into clinical experience. Cerebral centers of vesical control have been demonstrated in the corpus striatum, optic thalamus and motor area of the cortex by Czyhlary and Marburg; the center for tonic influence, in the mid portion of the pons by Barrington,[42] and the control of the tone of the vesical wall, in the region of the acoustic colliculus, according to Langworthy and Kolb.[43] Intactness of the cerebral control is necessary for normal function. The spinal urogenital centers are usually assigned to the level of the conus, the twelfth thoracic and the first, second and third sacral segments. Local control of the

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39. Alexander, F., and Staub, H.: The Criminal, the Judge and the Public: A Psychological Analysis, New York, The Macmillan Company, 1931.

40. (*a*) Rose, D. K.: Present Status of Cystometry, J. A. M. A. **107**:1534-1537 (Nov. 7) 1936. (*b*) Denny-Brown and Robertson.[38b]

41. Learmonth, J. R.: A Contribution to the Neurophysiology of the Urinary Bladder in Man, Brain **54**:147-176 (June) 1931.

42. Barrington, F. J. F.: (*a*) Central Nervous Control of Micturition, Brain **51**:209-220 (June) 1928; (*b*) Component Reflexes of Micturition in the Cat, ibid. **54**:177-178 (June) 1931.

43. Langworthy, O. R., and Kolb, L. C.: Encephalic Control of Tone in the Musculature of the Urinary Bladder, Brain **56**:371-382, 1933.

bladder is by the sympathetic system via the presacral nerve; by the parasympathetic system, via the pelvic nerves; by the voluntary system to the external sphincter, via the pudendal nerves, and by a local intrinsic nerve-net coordinating mechanism of the smooth muscle of the bladder which can work independently of its extrinsic nerve supply and which explains the development of automatic control of the bladder.[44] The sympathetic system controls largely the filling of the bladder and the contraction of the trigon; the sense of fulness on stimulation of the central end of its cut supply is interpreted as pain to some degree.

"Upon its resection, the bladder holds the same urine quantity at less pressure, and the emptying mechanism appears to be more efficient. There are two opposing forces reaching the bladder through the sympathetics; one produces a contraction of smooth muscle at the base of the bladder, and the other inhibits the detrusor. The sympathetics are in no way essential for normal micturition."[38d]

Sterility in the male may result from presacral neurectomy owing to loss of enjaculatory nerve control.[44a] The parasympathetic supply largely controls the detrusor or emptying mechanism. Section of this supply on one side in the experimental animal[17] produces a one-sided thickening of the bladder, impaired emptying and severe irritability, but continence remains and the vesical volume becomes less. After bilateral parasympathectomy the bladder becomes irritable, and anesthesia of the perineum occurs, accompanied by rectal and vaginal prolapse. The capacity of the bladder becomes increasingly larger, and automaticity with retention may or may not develop. But in such cases presacral neurectomy (sympathectomy) decreases the irritability and capacity returns to near normal, the prolapse improves and the function of the automatic bladder is greatly improved. Such has been the experience clinically in cases of severe injury to the lower part of the cord[30] and of extreme spina bifida.[45] Sensory impulses from the mucous membrane are by way of sympathetic nerves. The pudic nerves control the external sphincter and are voluntary. Their section in women for pruritus[41] has not resulted in incontinence, and Rochet[46] found no incontinence in the male on bilateral resection, but Barrington described in the cat some weakness of the sphincter and dribbling on exertion. A recent communication[47] indicated rectal weakness on the ipsilateral

44. Zimmerman, I. J.: Neuromuscular Physiology of Detrusor Muscle of Urinary Bladder, J. Urol. **40**:766-788 (Dec.) 1938.

44a. Braasch, W. F., and Learmonth, J. R.: Resection of Presacral Nerve in Treatment of Cord Bladder, Surg., Gynec. & Obst. **51**:494-499 (Oct.) 1930.

45. (*a*) Smith, C. K., and Engel, L.: Neurogenic Vesical Dysfunction in Children, J. Urol. **28**:675-683 (Dec.) 1932. (*b*) Langworthy and Dees.[16]

46. Rochet, V.: (*a*) Chirurgie de l'urèthre, de la vessie, de la prostate, Paris, G. Steinheil, 1895; (*b*) Surgical Affections of the Lower Bladder, Lyon chir. **18**: 143-152 (March-April) 1921.

47. Huggins, C.; Walker, A. E., and Noonan, W. J.: Sympathetic and Pudendal Neurectomy for Vesical Atony, J. Urol. **41**:696-715 (May) 1939.

side and rare incontinence following unilateral section of the pudic nerve, with actual improvement in the preoperative incontinence.

The roentgen studies of Ortman and Christiansen [37a] and Blum [37d] showed that a normal bladder produces a uniform cystogram recognized as such. Serial vesicourethrograms of the excretory process revealed that in the male the bladder is functionally continent only as long as all parts of the closing mechanism remain intact, proving the functional oneness of the whole mechanism, internal sphincter, prostatic urethra and external sphincter. A uniform finding is that the prostatic urethra to be normal must be elastic both in caliber and in contractility and that it is definitely shortened in the act of normal micturition. When such findings are absent variances in retention or in incontinence occur. In regard to the female, Stevens [37b] has demonstrated roentgenograms to prove that a well supported urethra with fixation at the vesicourethral junction is necessary for normal continence.

Clinical cystometry offers the most practical method of determining the normal way in which the bladder fills with urine, or variations from the normal way, and of demonstrating the state of the retaining mechanism. Since Mosso and Pellacani [38a] first studied the action of a full bladder, by recording its fluctuating state on a smoked drum, until the present considerable knowledge of the bladder and sphincters has come from such study. We have found cystometry of some help in the analysis of reasons for enuresis. By cystometry one learns that normal desire to urinate is initiated by the pressure the vesical wall exerts on its contents rather than by the volume in the bladder and that the desire varies for each bladder in the normal or a pathologic state.[38b] As the normal bladder fills, intravesical pressure rises evenly until the desire to void occurs, after which there is a rapid rise usually as capacity is reached, and with the rise a deep discomfort. At capacity, in the normal bladder the sphincters should remain intact. As the subject voids, the following sequence occurs: a sharp rise in intravesical pressure, followed in a moment by opening of the neck of the bladder; then filling of the posterior portion of the urethra and opening of the external sphincter, followed by a sharp fall in pressure with a sensation of relief. Evaluation of these facts along with other findings permits an accurate conception of the intactness of the neurovesical pathways and of the local neurogenic and myogenic obstructive factors. Rose [40a] stated concerning this procedure:

> It is a sensory, vesical volume pressure with sphincter control diagnostic procedure. . . . The clinical value of this procedure lies chiefly in its identifying the bladder to clinicians as an organ of practical physiologic importance . . . and in offering bladder function tracings to explain symptoms and determine the results of treatment in dysuric bladders.

The literature concerning therapy and results is voluminous and until recent years was rather disorganized because of the lack of a rational approach. It is unnecessary to repeat here the excellent summaries by Anderson,[2] Gerard [48] and the Mowrers.[21a] General procedures of value have been the treatment of physical defects, the limitation of fluids, the administration of salt to patients who did not concentrate the night urine [49] and the judicious use of atropine, ephedrine, acetylbetamethylcholine hydrochloride (mecholyl) and sedatives. Specific therapy directed to train the inhibitory reflex has been rationally explained and successfully used only by the Mowrers [21a]; it is based on an earlier idea of Pfaundler.[50] This treatment employs an electrical apparatus that rings a bell when the child urinates. The child is aroused, and after a few nights ceases to void the entire content of the bladder, goes to the toilet and within two months has developed control. This is training a conditioned reflex. Our own therapy is based on the same training of a conditioned reflex but is carried out in a different manner. The correction of local genitourinary pathologic conditions is given credit by many, and digital massage of the trigon has its advocates. Psychotherapy has proved its usefulness and in proper hands has been successful.[51] Amberg [38c] made simple cystometric studies of enuretic patients, trying to determine whether enuresis is psychic. He recorded reactions of the bladder to filling, to voluntary expulsive efforts, to various emotional states and to effects of atropine administered hypodermically. He could not answer the question of the psychic factor but concluded that atropine is a useful drug in the treatment of irritable bladders.

Our own investigation of an enuretic child consists in taking a routine history by questions adapted to such a patient, performing a physical examination including laboratory and roentgenologic studies and making an analysis of the function of the bladder by cystometric and cystoscopic study when we believed that the patient would benefit from such exami-

48. Gerard, M. W.: Child Analysis as a Technique in Investigation of Mental Mechanisms Illustrated by Study of Enuresis, Am. J. Psychiat. **94**:653-663 (Nov.) 1937.

49. Krasnogorski, N. I.: New Ideas in Handling Nocturnal Enuresis, Monatschr. f. Kinderh. **57**:252-260, 1933.

50. Pfaundler, M.: Demonstration of an Apparatus for Signaling Wetting, Verhandl. d. Versamml. d. Gesellsch. f. Kinderh. deutsch. Naturf. u. Ärzte **21**:219, 1904.

51. (*a*) Hamill.[26] (*b*) Lewis, J. M., and Ostroff, J.: Psychic Enuresis in the Normal Child, Am. J. Dis. Child. **43**:1490-1496 (June) 1932. (*c*) Beverly.[25] (*d*) Feer.[5a] (*e*) Gerard.[48] (*f*) Gerard.[24] (*g*) Michaels, J. J., and Goodman, S. E.: Incidence and Interrelation of Enuresis and Other Neuropathic Traits in So-Called Normal Children, Am. J. Orthopsychiat. **4**:79-106 (Jan.) 1934; (*h*) footnote 1.

nation. The psychologic status is determined by questioning the child and the parents and in some instances by "play observation" of the child.

During the period of this study a chief complaint of enuresis occurred in less than 1 per cent of the new patients in this general children's clinic. Addis [31a] reported that 18.4 per cent of children coming to a London clinic presented a chief complaint of enuresis and were aged 8 to 10 years, with 3 boys to every 2 girls. Our patients' average age at the first visit was 9 years. One hundred children were used for this study; 63 were boys and 37 were girls. The histories disclosed that 47 of these patients had nocturnal enuresis with diurnal frequency but no diurnal incontinence; 41 had nocturnal enuresis but were otherwise normal; 10 had diurnal as well as nocturnal enuresis, and 2 had only diurnal enuresis, with normal nocturnal control. Addis reported 50 per cent of his patients had diurnal and 50 per cent nocturnal enuresis. Hubert [32] stated that only 12 per cent of his patients had both day and night enuresis. Fifty-nine of our patients had once acquired normal control as babies, at an average age of 16½ months for boys (33 cases) and 17½ months for girls (22 cases). Anderson [2] reported that in 20 per cent of his patients enuresis developed after the children had once had normal control. He also stated that 80 per cent of his patients had nocturnal enuresis only, 11 per cent both nocturnal and diurnal, 3 per cent diurnal only. Hubert reported 58 per cent had been incontinent since birth and 32 per cent began to show night incontinence at from 3½ to 5 years and 10 per cent in later years. Twenty-one of our patients stated they were normal in the summer but had enuresis when the weather turned cold (16 boys and 5 girls).

The analysis of heredity revealed that 63 of our patients gave histories of parents, and 21 of siblings, who had enuresis. Addis found that 16.6 per cent of fathers, 10 per cent of mothers and 20 per cent of siblings also had a history of enuresis. Intelligence rating by school progress demonstrated that 70 of our patients were average and that 15 were above and 15 below average. Some have reported [31a] that patients with enuresis are equally divided into above and below average groups rather than into average, above average and below average groups, another that there are 25 per cent in the subnormal group,[2] while Hubert [32] stated that 75 per cent were in the average group. In only 5 instances did parents know of a predisposing cause, such as illness or psychic trauma. In 20 instances there was home disruption, such as divorce or the death of one parent, and in 14 other instances, gross parental disharmony but not separation. Only 8 of our children came from institutions; the remainder lived at home except for 9 who lived with relatives. Fifty-three slept alone, 7 with parents and 40 with

siblings. There were 14 per cent "only child" families and 86 per cent "multiple children" families, with an average of 2.4 children to a family. When sleeping away from home 13 had no enuresis and 53 had enuresis the same as at home, while 34 had never risked sleeping away from home. Thirty-three had undergone treatment for enuresis before coming to us. We obtained no histories of allergy. Only 1 child reported abnormal, difficult delivery. As to the parents' efforts, 40 per cent had tried in a mild way to do something for the child, 44 per cent had never done anything previous to the visit to the physician, and only 16 per cent had made intelligent efforts. The attitude of the parents on the first visit was interesting to record, for 75 per cent talked despairingly and acted hopeless but came for advice because the "wetting" was such a nuisance they had to talk with some one about it, though not expecting any cure for the child.

The psychologic investigation showed cooperative attitudes in 64 of the patients, uncooperative in 8 and indifferent in 21; only 7 could be classed as definitely antisocial or delinquent; 52 showed marked degrees of timidity and sensitiveness, 38 had mild to marked infantile traits, 14 were considered untrustworthy or unreliable, 12 were of the "leader" and the remainder of the "follower" type, 28 showed some emotional problems. Grossly psychopathic states were present in only 2 patients.

The general and special examinations did not reveal as great an incidence of organic factors as reported by Campbell.[7] Fifteen of the children showed subnormal physical characteristics, being underweight or anemic, and 2 had active tuberculosis. Three had cryptorchidism, 23 had pinhole external meatus (in only 3 was it a primary cause, however), 3 of the girls under 11 years of age had patent hymen, 1 had a small rectal fissure. No abnormal neurologic conditions were encountered other than impaired perineal sensations in 2 children with myelodysplasia. When asked to stop and start the urinary stream on command, after they became friendly toward the examiner, 81 of the children were able to do so. No positive Wassermann or Kahn or Hinton reaction of the blood serum was obtained. Urinalyses revealed abnormal urine in only 5 cases. A failure to concentrate night urine (specific gravity) was found in 5 patients. Cystometric analysis was done for 90 patients and gave normal results for 53 and abnormal for 37. It was considered to be of help in diagnosis in 80 cases and of no value in 10. Residual urine was encountered in 3 boys only. Cystograms were made for 80 patients and were found normal in 72 instances. Roentgenograms were made for 85 patients, and 46 per cent showed some degree of spina bifida occulta. Cystoscopic examination was performed for 45 patients and found to be of help in diagnosing the condition in 20.

The analysis of our records leads us to suggest the following classification of enuresis based on cause. The frequency of each type in our series is indicated:

			Cases
I. Organic (13%)	Local	Sclerosis of the neck of the bladder (observed in males)	2
		Congenital weakness of sphincter (observed in a 5 year old girl. An operation was performed)	1
		Hypertrophy of the verumontanum	2
		Congenital posterior urethral value (observed in a male)	1
		Rectal fissure	1
		Pinhole external meatus	3
	General	Endocrinopathy	1
		Tuberculosis, renal	2
II. Neuromyogenic (37%)		Conditioned reflex	21
		Neuromuscular imbalance of sphincter	13
		Myelodysplasia	3
		Pathologic condition in central nervous system	0
III. Psychogenic (50%)			

The only classification needing some clarification is the conditioned reflex type of neuromyogenic disturbance. This group includes children who at the first cystometric analyses responded vaguely to questions concerning sensations and their localization and who had never had normal control. With repeated cystometric study and encouragement they improved in control and reactions. It seemed to us that they thus developed, or established more firmly at least, a neural pathway and cerebral interpretation of vesical function.

The use of mechanical methods in diagnosis with these children, such as cystometry, cystography and cystoscopy, has met no objection on the part of parent or child, and has been of distinct help. Also it cannot be denied that a strong psychologic stimulus is often incidental. The demonstration to the child that he can actually hold all the water injected, and control its voiding, is encouraging to him. Adequate gentleness and anesthesia will induce any child to trust the investigator. Cystometric analysis, although time consuming, has been of considerable help as a functional diagnostic aid, and ranks high as a therapeutic procedure, by correctly conditioning vesical reflex control and cerebral interpretation and by altering vesical spasticity due to an overactive detrusor. This procedure does for us in training the bladder what the

signal apparatus of Mowrer [52] does in conditioning the reflexes of his patients. Cystograms and cystoscopic examination, we now believe, are indicated only in the presence of abnormal cystometrograms, urinary retention and infection.

The treatment was based on, first, the establishment of a correct diagnosis. To be sure, it is impossible to make accurate diagnoses without some failure, but as we progressed the results indicated that judgment became skilful enough to produce, for all practical purposes at least, a majority of correct working diagnoses on which to plan treatment. In a discussion of the therapy of enuresis, a symptom which is the local manifestation of so many types of functional as well as organic disease conditions, dogmatic statements cannot be made. In a case of organic disease it may be necessary not only to correct the abnormal condition but to train the patient into normal vesical control. A patient with a psychogenic condition could be thoroughly worked on from that point of view alone and failure ensue because of neglect of so simple a thing as a meatal stricture. For the child who has been proved quite normal in all examinations and whose enuresis is considered to be of the psychogenic type, it is an error to insist on drug or mechanical therapy, because the eventual cure of this type of enuresis demands emotional adjustment and assumption of complete responsibility on the part of the child alone, without dependence on the doctor, drugs or parents. It is productive of best results to use several therapeutic aids, recognizing that most cases require a major effort in one direction but may need also some degree of training and emotional stimulation and stabilization.

A review of the results of our treatment shows 64 per cent of the patients cured (as determined by continued normal control six months after all treatment was discontinued), 21 per cent improved enough to satisfy parents, and voluntarily ceasing treatment (14 per cent of these required an occasional repetition of the therapy for a mild recurrence of symptoms), while only 15 per cent either failed to improve or stopped treatment and disappeared before we observed a cure. A few illustrative case histories are here presented because of their special significance.

REPORT OF CASES

CASE 1.—An organic defect was successfully corrected. This was encouraging to us because it converted a shy, seclusive, miserable little girl into one of the happiest youngsters we know and replaced her in society to some usefulness.

A girl aged 9 years, who had always had enuresis both day and night with diurnal frequency, was timid and below average mentally. She had been denied two years of school because of her diurnal enuresis. The only positive

52. Mowrer, O. H.: An Apparatus for Study and Treatment of Enuresis, Am. J. Psychol. **51**:163-166 (Feb.) 1938.

finding was made on cystoscopic and cystometric analysis. The bladder was normal but the sphincter would relax at practically no increase of vesical capacity or pressure. No definite sphincter of the neck of the bladder could be seen to close over the cystoscope or the endoscope. Local treatment was unsuccessful, and an operation was performed which included suprapubic exposure, resection of a "V" from the floor of the neck of the bladder and suturing the edges to make a tight neck. (Similar and other types of surgical treatment have been described by various authors.[53]) Suprapubic and urethral catheters were worn ten days. About the time the patient was to have been dismissed an infection of the upper portion of the respiratory tract developed, followed by mastoiditis. This was treated by bilateral surgical drainage, with good recovery. After the patient returned home, no urinary control seemed to develop. By aqueous distention of the bladder to just beyond the capacity producing the desire to void and by withdrawing the catheter and having the child "hold" until permitted to empty, and having her empty the bladder every two hours by the clock, we gradually developed control, and four months postoperatively the child was in school and continent, with normal night control, although she got up by herself once each night.

The organic types of enuresis are self explanatory when local urogenital causes are determined. Among the general causes, endocrinopathy was observed only once:

CASE 2.—A girl of 12 years had definite myxedema. Glandular therapy, administered in the medical department, improved her condition generally, but did not alter her enuresis. Simple training plus one aqueous distention of the bladder induced normal control.

CASES 3 AND 4.—In the 2 tuberculous patients, one was known to have tuberculosis and was being treated for that disease; following unilateral nephrectomy, his enuresis ceased. The other, a Negro boy of 12 years who had no complaints of any kind except that he had had enuresis all his life, was found to have a tuberculous bladder and renal involvement.

CASE 5.—Chart 1 is the cystometrogram of R. H., a boy 14 years of age, who had always had nocturnal enuresis except for a few nights in the summer. It represents essentially normal findings except for a strong terminal contraction at capacity, and on repeated tests the patient could rarely inhibit the imperative desire to void. We classified this enuresis as neuromyogenic with a poorly developed inhibitory response or an insufficiently conditioned reflex. The boy's history and physical findings were normal; he was well developed and cooperative. Studies of the sphincter showed it to be normal. Success followed aqueous dilation, training to hold (inhibit) and administration of small doses of atropine. On the eighteenth night after the first treatment the patient went without urinating and, except for a few "spill overs," became consistently normal within one month. Two bladder dilations, a week apart, were performed.

CASE 6.—Chart 2 is a cystometrogram of L. S., an 11 year old boy, who had always had nocturnal enuresis and occasional diurnal incontinence from imperative desire to urinate. His history and the physical findings were normal except that

53. (*a*) Gayet, R.: Therapy of Essential Incontinence in Young Girls by Drawing Vesical Sphincter Tighter: The Marion Operation, Lyon méd. **161**:285-294 (March 13) 1938. (*b*) Graf, P.: Surgical Therapy of Bedwetting, Zentralbl. f. Chir. **65**:883-887 (April 16) 1938.

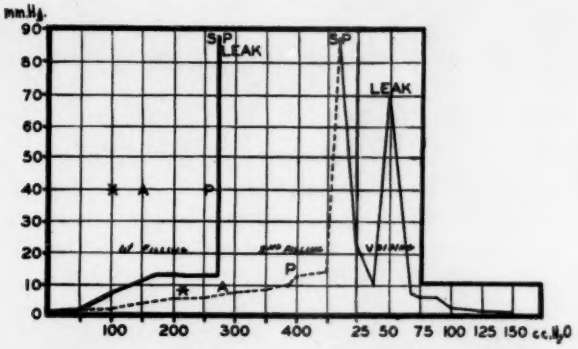

Chart 1 (case 5).—Cystometrogram of a patient with neuromyogenic enuresis. The asterisk indicates the first desire to void; *A*, anesthesia for lessening of desire to void; *P*, early pain of fulness; *SP*, pain at total capacity. Studies of the sphincter control revealed:

	Pressure in Bladder, Mm. Hg.	Pressure in Urethra, Mm. Hg.
At rest	18	0
Void	14	4
Stop	10 to 4	6 to 1

Filling was at low pressure with normal sensations and capacity but with a terminal spasm which the child could not control at capacity. The sphincter leaked on the first but not on the second filling except as the patient tried to inhibit the strong expulsive contraction. The voiding was normal. Successful therapy consisted of: aqueous dilation plus administration of atropine to tolerance.

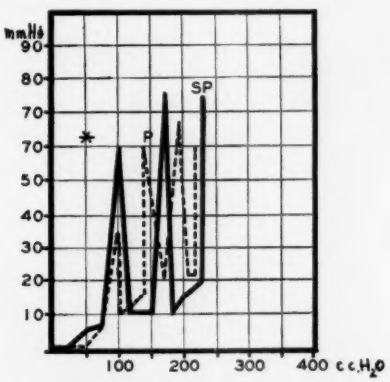

Chart 2 (case 6).—Cystometrogram of a child with enuresis. (See legend of chart 1 for explanation.) Studies of the sphincter control at 100 cc. revealed:

	Pressure in Bladder, Mm. Hg.	Pressure in Urethra, Mm. Hg.
At rest	8	0
Void	8 to 60	30
Stop	40-60 to 12	25 to 12

There was typical spastic response to distention, and rather high intracystic pressure was required to open the neck of the bladder. Successful therapy consisted of: passage of a large catheter, aqueous distention of the bladder every seven days and administration of atropine to tolerance.

he was a little underweight and shy and self conscious about his enuresis. The urinalysis and cytoscopic and cystographic findings were normal except that they exhibited confirming evidence of the spasticity of the bladder. No myelodysplasia was evident. This represented to us an overbalance of the emptying mechanism, probably parasympathetic, although we may be permitted to consider some factor within the vesical wall to be responsible for the strong contractions he could not inhibit. Observation at night, by means of a large condom, indicated that he voided 50 to 100 cc. of urine when asleep, evidently on the occurrence of the first desire to void, at the first strong contraction. Studies of the sphincter indicated that he had a rather high intracystic pressure before the neck of the bladder opened, but we could find no tightness, and repeated analysis later demonstrated normal pressure ranges. This patient responded to treatment (one aqueous dilation to capacity every seven days plus gradual administration of atropine to tolerance) by having no diurnal incontinence on the fourteenth day and no trouble thereafter in the day. The nocturnal enuresis was slower to respond, but on the nineteenth night after the first treatment he went for the first time without voiding. He occasionally had slight "wettings" for the next month, then became satisfied with his progress and refused further treatment. Four months later he began to urinate at night as before treatment. One distention evidently corrected the faulty coordination, and the patient was normal for another three months, at the end of which time there was another series of nights in which he urinated. One distention plus administration of atropine again resulted in good control. He was normal at the last contact, a year subsequent to the last treatment.

In treating patients with neuromyogenic enuresis, 4 types of bladders of interest were encountered. A type giving a rather normal-appearing cystometrogram, with a terminal sudden elevation of intracystic pressure and imperative impulse to void that may or may not be successfully inhibited, similar to that represented in chart 1, which we have described, was fairly common. When a bladder was of this type the enuresis was usually placed in our classification as proceeding from a poorly conditioned reflex. We occasionally saw an atonic bladder of large capacity, with or without some physiologic obstruction (tightness) at the neck of the bladder (chart 3). A type just the opposite, with a small capacity and high intracystic pressure, with or without a similar bladder neck, indicated that the detrusor was overactive as compared with the holding (sphincter) mechanism. There was one other type of interest—the bladder that demonstrated spasticity and irritability with unsuccessful inhibition of the involuntary expulsive contractions (chart 2). The latter 3 types we grouped as neuromuscular-sphincter imbalance types.

In the treatment of the first of these types, good therapeutic results have followed aqueous distention of the bladder to the point of discomfort and asking the child to "hold" until allowed to void. This is done once or twice a week. When voiding, the child must stop the stream on command almost as soon as he is allowed to void. At home he is to practice "holding;" he is to go to the toilet when the desire arises but not to void until he has tried to subdue the desire. If he is successful, he is to wait until the desire comes again, whether it is in

five minutes or an hour. In this manner, we attempt to strengthen the neurovesical pathway of inhibitory control by conscious strong-willed effort in the hope it will carry over into the sleeping state. The results in some cases are encouraging. In others a strong effort has to be made to stimulate cooperation on the child's part. Atropine has been of help in minimizing the strong detrusor effect.

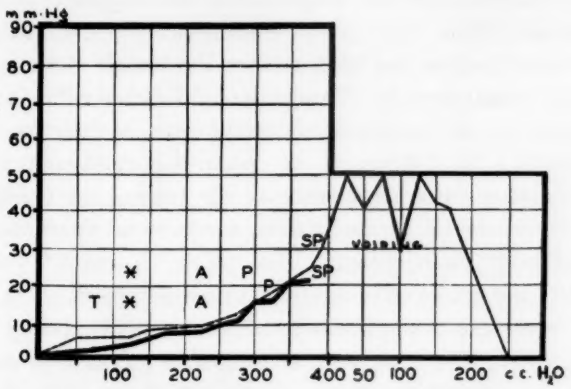

Chart 3.—Cystometrogram of a bladder that was moderately atonic, although the terminal pressure was near normal and voiding indicated that the bladder was required to make a strong expulsive effort to open the vesical neck or sphincters. (See legend of chart 1 for explanation; *T* indicates perception of temperature.) Studies of the sphincter control at 100 cc. revealed:

	Pressure in Bladder, Mm. Hg.	Pressure in Urethra, Mm. Hg.
At rest	18	0
Void	50	13
Stop	40 to 18	18 to 0

The voluntary voiding pressure was 68 mm. of mercury. The posterior part of the urethra and the neck of the bladder were found to be rigid and spastic. Successful therapy consisted of a few dilations of the posterior part of the urethra and of the neck of the bladder and simple training methods.

In the treatment of the atonic bladder we have had success by gentle dilation of the neck of the bladder with sounds and by irritation of the trigon, applying silver nitrate to it to induce frequent and strong emptying. Mecholyl (acetylbetamethylcholin) therapy produced a decrease in vesical capacity and an increase in the tone of the bladder wall in the 2 cases in which that method was tried. Gernon, Palmer and McKenna [54] have had good success in treating neurogenic enuresis in

54. Gernon, J. T.; Palmer, E., and McKenna, C. M.: Some Recent Developments in Treatment of Neurogenic Dysfunction of the Bladder Based on Cystometry, J. Urol. **35**:515-519 (May) 1936.

adults, using mecholyl to decrease the bladder's capacity. In treating a few of their tabetic patients, they obtained even better success with 4 mg. of ergotamine tartrate (N.N.R.) daily. Other drugs stimulating expulsion have not been tried by us, but Creevy [55] in some cases of large capacity and poor sensation with a normal condition of the sphincters, advised emptying by the clock at regular intervals (sometimes using an indwelling catheter temporarily) and a judicious use of pilocarpine, acetylcholine and acetylbetamethylcholine. The physiologic effects of acetylcholine and atropine are thoroughly discussed from an experimental standpoint by Henderson and Roepke.[56] Aqueous distention or the use of atropine is contraindicated in the treatment of this type of bladder. In 2 instances we obtained normal control only after the use of mild galvanic stimulation of the base of the bladder and the perineum at five day intervals for four weeks in addition to the therapy already outlined. Both patients were boys, 15 and 17 years of age. Sorrentino [57] and others have advocated this therapy in some cases.

In the treatment of the bladder exhibiting small capacity and strong detrusor activity, one finds that considerable increase in capacity and diminution in contractile power at capacity follow biweekly aqueous distention, controlled by cystometric analysis. Rose [40a] described a girl of 18 years who required periodic aqueous dilations of the bladder because of decreasing capacity and enuresis. In the presence of an overactive or tight neck of the bladder, simple dilation with a sound induces improvement. A sound designed by one of us (C. K. S.) for dilating strictures in children was used for this purpose. For children with poor sphincter control and slow conscious inhibitory effort, we tried many drugs acting as stimulants of the sympathetic nerves, and found morphine sulfate in syrup in physiologic doses, given at bedtime only, over a two to three week period, very efficient. We have had no satisfactory results using ephedrine, as suggested by Christopherson and Broadbent.[58]

In the treatment of the spastic bladder, cystometric analysis, repeated distentions, holding exercises and the use of atropine to tolerance have given encouraging results in from three to five weeks. The atropine

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55. Creevy, C. D.: Treatment of Overflow Incontinence of Neurogenic Vesical Dysfunction, J. Urol. **35**:507-514 (May) 1936.

56. Henderson, V. E., and Roepke, M. H.: Role of Acetylcholine in Bladder Contractile Mechanism and in the Parasympathetic Ganglia, J. Pharmacol. & Exper. Therap. **51**:97-111 (May) 1934.

57. Sorrentino, M.: Marconitherapy in Essential Incontinence, J. d'urol. **44**: 501-502 (Dec.) 1937.

58. Christopherson, J. B., and Broadbent, M.: Ephedrine and Pseudoephedrine in Bronchial Asthma and Enuresis, Brit. M. J. **1**:978-980, 1934.

exerts a satisfactory inhibitory effect on the parasympathetic or emptying control. Van Duzen [37c] has described this type of hypertonic detrusor effect and has used similar treatment.

Of the patients with extreme degrees of spina bifida, in only 3 could we consider the anomaly as the cause of the enuresis. The cystograms outlined the usual funnel neck bladder. The cystometric analysis revealed large capacity, low pressure and in 1 bladder a relaxed sphincter with poor detrusor force, findings similar to those of Langworthy and Dees.[16] We have seen no patients who have had laminectomy and neurolysis, and agree that one should be extremely cautious against a resort to operation except when the condition is intractable, as suggested by Mertz.[13]

In studying enuresis of the psychogenic type, we found numerous factors present and believe many of the causes reviewed in our discussion of the literature are acceptable. The enuresis in our patients we felt was a symptomatic expression in most instances of poor training, a conduct disorder, a psychopathic personality or a wish for attention associated with feelings of fear and inadequacy. In a few instances it was viewed as part of the problem of delinquency or as a physical manifestation of deep-seated anxieties or hates. In one instance, that of an older girl, it was associated with kleptomania, both exhibitions apparently being symptoms of thwarted drives. Bornstein [59] has discussed this particular problem from this and other points of view. Briefly, the best results have followed when we treated the child suffering from psychogenic enuresis as our equal and left the parents out of the affair entirely. At the first conference we tried to establish ourselves as the child's new and honest friends; hence he had a strong desire to do successfully for us what he would not do for parents who he already knew expected him to fail. We explained to the child that he could become "dry" any time he wanted to and could be responsible for conduct during sleep. Successful emotional training and adjustment of school and home problems are important. Suitable patients can best be handled by the psychiatrist interested in children. Of the 52 children with enuresis of the psychogenic type, 46 were improved or cured.

It is unfair to believe that there is distinct specificity in the treatment of enuresis. It is a better rule to direct the treatment toward methods that have been used successfully in the treatment of the type of enuresis one believes the patient to have. General therapeutic methods are justifiable also. We shall here outline a few that have been of some use to us: In all cases we advise that the drinking of fluids be eliminated after 6 p. m. and that supper be a concentrated and not a fluid meal.

59. Bornstein, B.: Enuresis and Kleptomania, Ztschr. f. psychoanal. Pädiat. **8**:229-236, 1934.

The bladder is to be emptied before going to bed. If the patient wets the bed, he is to be aroused each night thereafter at about the time he usually does this and made wide awake while an alarm clock rings loudly. This procedure is to be repeated a few nights until he rouses at the alarm alone and goes to the toilet by himself. No one is to assist him after the first few nights, and after a week or two of conditioning he is not to have the alarm but is to try to awaken by himself. The waking device described and used by Mowrer [60] sounds more satisfactory as a conditioner of the urinary reflexes but we have had no personal experience in using it. With those children who do not concentrate the night urine, we have tried giving sodium chloride, 2 to 3 Gm. at bedtime [49] in peanut butter or on bread or in tablets, with no particular success. A few boys have found the wearing of a simple Cunningham penile incontinence clamp at night for a week or so highly successful. With the sleepy, slow child, benzedrine sulfate (N. N. R.) has been tried as a systemic stimulant, 2.5 mg. being given twice daily, with some success. For restless sleepers simple sedatives have sufficed. We have not found our patients to sleep any more soundly than the ordinary child. This agrees with the findings of Courtin.[61]

SUMMARY

This study of 100 enuretic children observed in the clinic of a children's hospital embraces (1) a résumé of the psychosomatic significance and types of enuresis, known facts about bladder function, therapeutic methods and results described in recent literature; (2) the results of examinations (physical, laboratory, cystometric, urographic, cystoscopic and psychologic) of our patients, our method of classification and the results of treatment.

Enuresis in our experience was of 3 types: organic, 13 per cent; neuromyogenic, 37 per cent, and psychogenic, 50 per cent.

Diagnosis of the type of enuresis before instituting therapy is extremely important.

A simple cystometric examination was a distinct aid in the analysis of function.

Our series consisted of 63 boys and 37 girls. The average age was 9 years. In 59 who later had enuresis normal control had once developed, at the age of 16½ months in boys and 17½ months in girls. Forty-one had nocturnal enuresis only; 47 had nocturnal enuresis plus diurnal frequency but not incontinence; 10 had diurnal as well as nocturnal enuresis, and 2 had diurnal but not nocturnal enuresis.

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60. (*a*) Mowrer.[52] (*b*) Mowrer and Mowrer.[21a]

61. Courtin, W.: Relations Between Enuresis and Sleep, Arch. f. Kinderh. **73**:40-50 (June) 1923.

Therapeutic methods in addition to correction of physical defects and simple training methods are:

For spastic bladder, atropine therapy plus aqueous distention.

For atonic bladder, stimulation of the neck of the bladder and in severe cases mecholyl (acetylbetamethylcholine) and acetylcholine.

For strongly expulsive bladder of small capacity, simple regular aqueous distention.

For nocturnal enuresis plus poor sphincter action, physiologic dosage of morphine at bedtime only.

Treatment was directed toward establishing a conditioned reflex by developing in the child a strong conscious effort to control the distended bladder, an effort which establishes neural pathways and cerebral interpretation of vesical function. This treatment worked best on essentially normal bladders.

Patients with definite psychogenic enuresis responded well to simple psychotherapy, encouragement, education and adjustment of personal and social problems.

Results indicated that 64 per cent of the patients were cured and 21 per cent improved (14 per cent of whom had recurrences occasionally); 15 per cent were classed as unsatisfactory for various reasons.

505 Professional Building.

TUBERCULOSIS

A FOLLOW-UP STUDY OF CHILDREN AT LYMANHURST HEALTH CENTER

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Throughout the years the Lymanhurst Health Center has been in operation sustained efforts have been made to obtain periodic follow-up studies of the children examined there for tuberculosis. Consequently, since 1921, the year Lymanhurst was established, a considerable volume of data of increasing value has accumulated. This report presents an analysis of the records of 10,003 children who entered the clinic between May 1921 and July 1932.

RESULTS OF INITIAL EXAMINATION

General orienting information relative to the results of the initial examinations is provided by table 1. Since the Mantoux test replaced the Pirquet test during the period covered by this study, the data recorded in this table are separated according to the type of test used and the result each test yielded. Inspection of the records compiled on this basis shows that the principal roentgenographic differences observed between the two uninfected as compared with the two infected groups of children paralleled the character of the reaction to tuberculoprotein rather than the type of test that was used. Discussion of the results of the initial examinations these patients received may be confined, therefore, chiefly to the combined data listed in the last three columns of table 1.

The ages of the 10,003 children included in this study ranged from 3 months to 20 years and averaged 9 years. The mean age of the patients who were sensitive to tuberculoprotein (10.1 years) was slightly higher than that recorded for the group with negative reactions (8.6 years). The percentage distribution of the two groups of children according to age is shown in table 2, which discloses a consistent relative preponderance of older children in the infected group as compared with the uninfected group.

From the Lymanhurst Health Center and the Department of Pediatrics, University of Minnesota.

At the time of the initial study, roentgen examinations were made of the chests of 95.5 per cent of the 2,896 infected patients and of 84.3 per cent of the 7,107 children who entered Lymanhurst with negative

TABLE 1.—*Results of the Initial Examination of 10,003 Children*

	Negative Reaction		Positive Reaction		Both Tests		
	Pirquet Test	Mantoux Test	Pirquet Test	Mantoux Test	Negative Reaction	Positive Reaction	Summary
Number of children	4,887	2,220*	2,042	854	7,107	2,896	10,003
Average initial age (yr.)	8.5	8.9	9.8	10.6	8.6	10.1	9.0
Number examined roentgenographically	4,576	1,413	1,919	848	5,989	2,767	8,756
Percentage examined roentgenographically	93.6	63.6	94.0	99.3	84.3	95.5	87.6
Results of first roentgen study of lungs							
Incidence of normal lungs	4,280 (93.5%)	1,281 (90.7%)	1,140 (59.4%)	437 (51.5%)	5,561 (92.9%)	1,577 (57.0%)	7,138
Incidence of nontuberculous lesions	167 (3.6%)	91 (6.4%)	78 (4.1%)	51 (6.0%)	258 (4.3%)	129 (4.7%)	387
Incidence of primary tuberculous lesions							
Pneumonic	0	0	109 (5.7%)	57 (6.7%)	0	166 (6.0%)	166
Calcified or fibrosed	129 (2.8%)	41 (2.9%)	562 (29.3%)	284 (33.5%)	170† (2.8%)	846‡ (30.6%)	1,016
Incidence of chronic pulmonary tuberculosis	0	0	30 (1.6%)	19 (2.2%)	0	49 (1.8%)	49

* Four children had negative reactions to 0.01 mg. of old tuberculin, 1,108 to 0.1 mg. and 1,108 to 1 mg.
† These include 167 instances of calcification and 3 of fibrotic infiltration.
‡ These include 826 instances of calcification and 20 of fibrotic infiltration.

TABLE 2.—*Percentage Distribution of Children According to Age*

Age in years..	0-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18-20
Percentage in each age group 7,107 children with negative reactions to tuberculin	2.6	3.1	4.9	5.1	5.7	6.9	9.4	9.4	8.6	7.0	6.7	6.5	6.0	5.5	5.1	4.3	1.9	0.9	0.6
2,896 children with positive reactions to tuberculin	0.9	1.7	3.2	3.3	3.7	5.1	6.0	7.9	7.9	7.7	8.3	8.5	8.2	8.1	7.8	6.5	2.9	1.3	0.8
Data for the two groups combined	2.1	2.7	4.4	4.6	5.2	6.4	8.4	8.9	8.4	7.2	7.2	7.1	6.6	6.2	5.9	4.9	2.2	1.0	0.6

reactions to tuberculin. The general policy of not using this relatively expensive type of examination for persons with negative reactions to tuberculin was adopted after study of roentgenograms of the chests of several thousand children consistently failed to reveal evidence of clinical tuberculosis in patients with negative reactions to tuberculin. Although practice of this economy reduced the incidence of roentgen

studies for the uninfected group included in this series, nevertheless the per cent of persons with negative reactions to tuberculin who received roentgenographic examinations (84.3 per cent) seems sufficiently high to provide a fairly accurate estimate of the prevalence and character of the intrathoracic pathologic conditions which can be demonstrated roentgenographically in children who are not sensitive to tuberculoprotein. After several years of experience in reading plates at Lymanhurst, Dr. J. R. McNutt reinterpreted the roentgenograms of the children included in this study. These final readings were used in the tabulations that were made.

Results of Initial Roentgen Studies.—The initial roentgenograms were interpreted as revealing normal lungs for 92.9 per cent of the children with negative reactions and for 57 per cent of those with positive reactions. The incidence of pathologic changes revealed by roentgen study of the uninfected children obviously fell far short of that disclosed by the roentgenograms of the infected patients.

Distinctly increased bronchovascular markings, bronchiectatic changes, pulmonary cysts and various other lesions which were interpreted as nontuberculous were revealed in 4.3 per cent of the roentgenograms of the children whose reactions to tuberculin were negative and in 4.7 per cent of those of the infected group. No significant difference was noted, therefore, between the two series of children with respect to the incidence in each of roentgenographically demonstrable nontuberculous changes. All of the remaining lesions which the roentgenologist reported for the two groups of children were of the type which the tubercle bacillus produces.

Relatively benign pneumonic infiltrations were found in 166 members of the infected group. Repeated roentgen studies made of 141 of these patients (table 4) disclosed a general tendency for the infiltrations first to persist for months without exhibiting conspicuous gross changes and later to undergo a spontaneous resolution, which led gradually either to their complete disappearance from the roentgenogram or to their reduction to trivial calcified or fibrosed deposits. No similarly benign lesions which persisted for months before resolving were found in the children whose reactions to the tuberculin test were negative. The uniform clinical and roentgenographic characteristics of the relatively persistent pneumonic infiltrations found only in tuberculin-sensitive children, the concentration of such lesions chiefly in the younger age groups (chart 1 *B*) and the frequency with which they ultimately produced deposits interpreted as calcium are some of the factors which served to identify these infiltrations as signs of primary pulmonary tuberculosis in the early pneumonic stage of development.

Initial roentgen studies of 5,989 children with negative reactions to tuberculin revealed changes interpreted as calcium deposits in 167 children and as fibrotic deposits in 3. For the uninfected group the incidence of these intrathoracic lesions which were roentgenographically indistinguishable from like changes commonly produced by primary tuberculous infections amounted to 2.8 per cent. The incidence of similar lesions for the tuberculin-sensitive children (30.6 per cent, that is 826 children with calcium deposits and 20 with fibroid deposits) was more than tenfold that recorded for the children with negative reactions to tuberculin. The relatively high incidence of calcium deposits, revealed roentgenographically in the tuberculin-sensitive group is correctly attributable, no doubt, chiefly to the infections with tubercle bacilli which these children had experienced. The calcified and fibrosed intrathoracic lesions present in 30.6 per cent of the 2,767 infected patients for whom initial roentgen studies were made are interpreted as indicating a later stage in the evolution of primary pulmonary tuberculosis than was represented by the relatively persistent pneumonic infiltrations found in 166 infected patients.

At the time of the first examination, disease diagnosed as chronic pulmonary tuberculosis of the adult type was discovered exclusively in the tuberculin-sensitive group. Initial roentgen studies of 2,767 infected patients revealed 49 instances of this form of the disease, a condition which I interpret as representing the second of the two phases of the evolution of pulmonary tuberculosis which can be recognized in living patients. In this group of children the incidence of the second developmental stage was about one twentieth the incidence of all of the roentgenographically demonstrable changes interpreted as exemplifying different stages of the primary phase.

Of the 2,767 tuberculin sensitive children for whom initial roentgen studies were made, a total of 38.3 per cent had roentgenographically demonstrable lesions which were considered tuberculous (the primary tuberculous pneumonic infiltrations, the calcified and fibrosed deposits and the chronic ulcerative pulmonary tuberculous lesions combined), whereas 4.7 per cent had pathologic changes which were interpreted as nontuberculous. These observations indicate conclusively that with respect to an ability to produce persistent intrathoracic changes which cast shadows in roentgenograms, the tubercle bacillus occupies a unique position among the different bacteria which cause pulmonary disease during childhood.

Variations in Roentgenographic Findings at Different Ages.—The variations at different ages in the incidence of the several types of lesions which were revealed by the initial roentgen studies of the uninfected and also of the infected children are portrayed graphically by

chart 1. Inspection of this graph discloses that for the children with negative reactions to tuberculin the incidence of the lesions which were considered definitely nontuberculous as well as that of the calcified and fibrosed deposits tended in general to increase with advancing age, but in only a few of the older groups did their combined incidence exceed 10 per cent. The occasional presence in the uninfected group of roentgenographic evidence of calcified and fibrosed deposits which were indistinguishable from similar changes commonly produced by primary

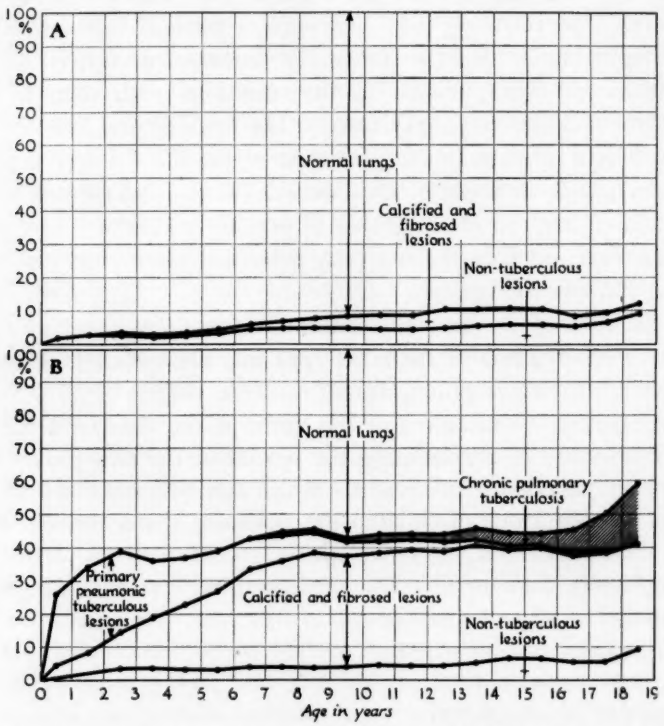

Fig. 1.—*A*, results of the initial roentgen studies of 5,989 children with negative reactions to tuberculin, and *B*, results of the initial roentgen studies of 2,767 children with positive reactions to tuberculin.

tuberculous infections may be attributed, perhaps, to errors in the interpretation of roentgenograms, to the production of lesions of this kind by some nontuberculous infections or to the loss of sensitivity to tuberculin in a few instances. Fortunately the incidence of shadows in roentgenograms which may be confused with those representing changes commonly produced by the tubercule bacillus is low (about 2.8 per cent) for Minneapolis children with negative reactions to tuberculin.

The curves representing the conditions revealed at successive ages by the initial roentgen studies of the infected group (chart 1 *B*) differ

conspicuously from those representing the condition disclosed by the roentgenograms of the uninfected group. Inspection of the curves reveals that this difference consists not only in the presence of primary pneumonic tuberculous infiltrations and of chronic pulmonary tuberculosis exclusively in the infected series but in a relatively high prevalence of calcified and fibrosed lesions in this group.

The pneumonic infiltrations which were considered representative of the introductory inflammatory stage of primary pulmonary tuberculosis occurred with greatest frequency in the infected children who were less than 3 years of age. During this age the incidence of such lesions definitely exceeded that of the other types of pathologic condition revealed by roentgenograms. Although the percentage of infected children with roentgenographically demonstrable primary pneumonic tuberculous infiltrations diminished rapidly after the age of 3 years, lesions of this character were found throughout practically the entire period of childhood.

The percentage of roentgenographically demonstrable calcified and fibrosed lesions increased rapidly in the infected group until the age of 8.5 years. Thereafter the incidence of such lesions displayed no consistent change. Throughout the major portion of childhood calcified deposits constituted the most common type of pathologic change revealed by roentgenograms of tuberculin-sensitive patients.

The incidence in different age groups of chronic pulmonary tuberculosis of the adult type which the initial roentgen examination disclosed is indicated by the shaded zone in chart 1. This type of tuberculosis made its appearance in the infected patients during the seventh year of life and tended in general to increase in relative frequency in each successive age group.

Since the striking roentgenographic differences observed between uninfected and infected groups of children of corresponding age consisted primarily in a relative abundance in the latter of roentgenographically demonstrable intrathoracic changes which were interpreted as tuberculous lesions, it seems reasonable to conclude that these differences were caused chiefly by the presence of infections with virulent tubercle bacilli in one group and the absence or scarcity of such contaminations in the other group.

RESULTS OF FOLLOW-UP STUDY

General information relative to the scope and results of the follow-up study made of the children included in this series is provided by table 3. According to the records, 5,747 children, or 80.9 per cent of those with negative reactions to tuberculin, and 2,467 children, or 85.2 per cent of the infected patients, were traced. Of the children with negative reactions to tuberculin who were traced, 46.5 per cent were repeatedly

examined roentgenographically. An additional 25.4 per cent of this group was retested with tuberculin but was not reexamined roentgenographically owing to the fact that the reactions to the second series of tests were negative. The follow-up data of the remaining 28.1 per cent of the traced children who entered Lymanhurst with negative reactions to tuberculoprotein were limited to verbal information which indicated apparent health and disclosed whether the children were living or dead.

TABLE 3.—*Results of Follow-Up Study*

	Pirquet Test		Mantoux Test		Groups Combined Tuberculin Reaction		
	Negative Reaction	Positive Reaction	Negative Reaction	Positive Reaction	Negative	Positive	Total
Number of children studied	4,887	2,042	2,220*	854	7,107	2,896	10,003
Number traced	3,970	1,713	1,777	754	5,747	2,467	8,214
Percentage traced	81.2	83.9	80.0	88.3	80.9	85.2	82.1
Percentage of traced children reexamined roentgenographically	....	....	....	....	46.5	72.3	54.3
Percentage of traced children retested but not examined roentgenographically	....	....	....	....	25.4	0	17.8
Percentage of children traced by verbal data only	....	....	....	....	28.1	27.5	28.0
Average initial age, yr.	8.2	9.6	8.8	10.6	8.4	9.9	8.9
Average duration of follow-up period, yr.	7.1	7.8	3.9	5.0	6.1	6.9	6.3
Total person years of follow-up experience	28,073	13,297	6,926	3,790	34,999	17,087	52,086
Average age at end of study, yr.	15.3	17.4	12.7	15.6	14.5	16.8	15.2
Number who acquired chronic pulmonary tuberculosis	14†	51	2†	7	16	58	74
Incidence of chronic pulmonary tuberculosis							
Cases per 1,000 traced children	3.5	29.8	1.1	8.2	2.8	24.0	9.0
Cases per 1,000 person years	0.5	3.8	0.29	1.8	0.46	3.4	1.4

* Four of these children gave negative reactions to 0.01 mg. of old tuberculin; 1,108 to 0.1 mg., and 1,108 to 1 mg.

† Three children who originally gave negative reactions to the Pirquet test and 1 who originally gave a negative reaction to the Mantoux test later showed positive reactions, and pulmonary tuberculosis subsequently developed.

Of the infected children who were traced, 72.3 per cent were examined roentgenographically. Since retesting of children who were already known to be sensitive to tuberculin was seldom practiced at Lymanhurst, the reexaminations of the infected patients consisted chiefly in repeated roentgen studies. The follow-up information obtained for the remaining 27.5 per cent of the infected children who were traced was exclusively verbal and was equivalent to that obtained for 28.1 per cent of the children with negative reactions to tuberculin. In general, therefore, approximately 72 per cent of the children in each series of traced children received the type of reexaminations deemed necessary to disclose the presence or absence of clinical tuberculosis (either repeated tests or roentgenograms for the children with negative reactions to

tuberculin and repeated roentgen studies for the infected group). Verbal information concerning many of the children who were either retested or roentgenographically reexamined was obtained subsequent to the time of the last examination at Lymanhurst, and the date of the last information received was used in estimating the entire length of the follow-up period for these patients. Since follow-up data derived from roentgen studies, tuberculin tests and verbal inquiry were obtained on more than 80 per cent of the uninfected and infected children included in this study, the results of the investigation probably are significant.

The average initial age of the children who were traced amounted to 8.4 years for the uninfected group and 9.9 years for the infected group (table 3). The former were traced for an average of six and one-tenth years and the latter for six and nine-tenths years. At the end of the follow-up study the mean age of the tuberculin-sensitive children (16.8 years) was two and three-tenths years in excess of that (14.5 years) recorded for those with negative reactions to tuberculin. The total number of person years of follow-up experience amounted to 34,999 years for the uninfected group and 17,087 years for the infected group.

During the course of the follow-up period chronic pulmonary tuberculosis was acquired by 16 of the 5,747 traced children who entered Lymanhurst with negative reactions to tuberculin. For this group the incidence of this clinical variety of tuberculosis amounted to 2.8 cases per thousand children and 0.46 cases per thousand person years of follow-up experience.

Of the 2,467 traced children who entered Lymanhurst with positive reactions to tuberculin, 49 were found to have chronic pulmonary tuberculosis at the time of their initial examination. The remaining 2,418 members of the group presented no evidence of this form of disease when they first visited the clinic. During the course of the follow-up study chronic pulmonary tuberculosis was acquired by 58 members of the group. The incidence of newly developed chronic pulmonary tuberculosis observed for these 2,418 infected children amounted to 24 cases per thousand patients and 3.4 cases per thousand person years of follow-up experience. In general, therefore, the acquisition of this form of pulmonary tuberculosis occurred about eight times as frequently in the tuberculin-sensitive group of children as it did in the group of traced children who entered Lymanhurst with negative reactions to tuberculin. This observation is interpreted as conclusive evidence that the complex immunologic changes which infections with tubercle bacilli produce do not provide a satisfactory solution for the problem of human tuberculosis. Since infections with virulent tubercle bacilli perpetuate tuberculosis, the eradication of the disease seems to be strictly contingent on the prevention of contaminations with this organism.

Results of Follow-Up Roentgen Studies.—Follow-up roentgen examinations were performed on 2,670 of the children who entered

the clinic with negative reactions to tuberculin and on 1,784 of the infected patients. Each group was traced in this manner for an average period of approximately seven years, during which occasional roentgenographically demonstrable changes were observed in the lungs of uninfected children.[1] During the same interval marked changes were revealed by the serial roentgen studies of the tuberculin-sensitive group. Table 4 presents a summary of some of the more important changes observed in the lungs of the infected patients.

The incidence of normal lungs as revealed roentgenographically in the tuberculin-sensitive group decreased from 53.9 to 36.9 per cent during the seven year follow-up period. Since practically no change occurred in this interval in the frequency with which lesions that were considered nontuberculous were encountered, the shift in roentgeno-

TABLE 4.—*Results of the Follow-Up Roentgen Study of Infected Children*

	First Roentgen Examination		Last Roentgen Examination	
	Number	Per Cent	Number	Per Cent
Number of children examined roentgenographically	1,784	....	1,784	....
Average age, yr.	9.7	....	16.7	....
Total and average person years of follow-up experience	.....	....	12,492 (7.0)	....
Incidence of normal lungs	962	53.9	658	36.9
Incidence of nontuberculous lesions	68	3.8	59	3.3
Incidence of primary tuberculosis				
Pneumonic	141	7.9	12	0.7
Calcified and fibrosed	564	31.6	948	53.1
Incidence of chronic pulmonary tuberculosis	49	2.7	107	6.0

graphic findings in the infected group obviously concerned lesions that were interpreted as tuberculous.

Of the various roentgenographically demonstrable lesions which were attributed to the tubercle bacillus, only the pneumonic infiltrations of primary pulmonary tuberculosis displayed a tendency to decrease in frequency with advancing age. During the period of the follow-up study the incidence of such infiltrations decreased from 7.9 to 0.7 per cent. This change was the result of the slow process of spontaneous resolution which these lesions were observed to undergo. All of the remaining roentgenographically visualized lesions which were considered to be tuberculous increased in frequency during the course of the follow-up study.

At the conclusion of this investigation the incidence of calcified and fibrosed deposits recorded for the infected group had changed from an

1. In 16 patients chronic pulmonary tuberculosis developed and in a few additional patients pneumonic infiltrations and calcifications developed after the patients had acquired sensitivity to tuberculin.

initial 31.6 per cent to a final 53.1 per cent. A small part of this change resulted from the transformation of primary pneumonic tuberculous infiltrations into residual calcified deposits. The remainder of the increase was caused by the eventual appearance of roentgenographically demonstrable intrathoracic lesions of this general character in the lungs of many of the infected children whose initial roentgenograms revealed no evidence of pathologic conditions.

Chronic pulmonary tuberculosis of the so-called adult type was the remaining tuberculous lesion found with appreciable frequency in the

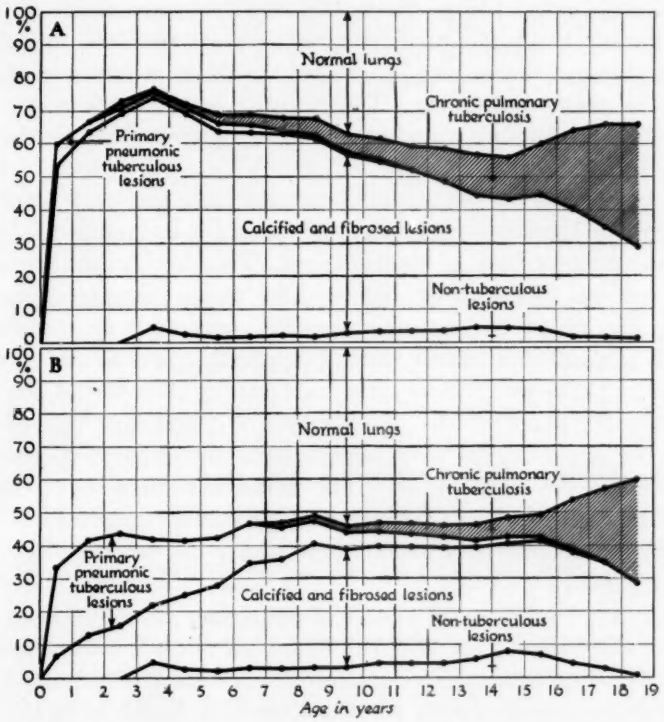

Fig. 2.—*A*, results of final roentgen studies made at the end of an average follow-up period of seven years on 1,784 children with positive reactions to tuberculin, and *B*, results of the initial roentgen studies of the same children.

lungs of the infected children. During the course of the follow-up study serial roentgenograms revealed an increase from 2.7 to 6 per cent in the group incidence of this form of the disease.

The pronounced shift in roentgenographic findings which occurred in the infected group during a period of seven years is portrayed graphically in chart 2, which provides a condensed picture of the principal roentgenographically demonstrable changes.

In general, the follow-up roentgen study of the tuberculin-sensitive children disclosed two broad successive phases in the evolution of pulmonary tuberculosis, the gross features of which can be observed and followed during the life of the patient. The more conspicuous features of the interrelated series of roentgenographically demonstrable changes which comprise the first phase of the evolution are the primary pneumonic tuberculous infiltrations and the calcified and fibrosed deposits. The former lesions are deemed representative of a comparatively early stage in the first phase of the development, whereas the calcified and fibrosed deposits are considered relatively old primary lesions. Many transitional changes bridge the gap between these two stages of primary tuberculosis. From the roentgenographic point of view, this developmental phase of the disease is featured chiefly by a tendency for acute lesions to calcify and fibrose. The evolution of the stage of the disease usually leads, therefore, to spontaneous retrogression and partial repair of the lesions.

The second of the two clinically demonstrable phases of development through which pulmonary tuberculosis passes is exemplified by chronic pulmonary tuberculosis of the adult type. This developmental phase, the gross features of which are revealed by serial roentgenograms taken during the life of the patient makes its appearance on the roentgenograms as small infiltrations which often tend to spread and to produce cavities. These progressive changes seem to characterize the second demonstrable phase of the development of pulmonary tuberculosis in much the same degree that retrogressive and reparative phenomena characterize the first phase. The commonly used terms minimal, moderately advanced and far advanced pulmonary tuberculosis roughly parallel the successive steps through which the second phase of the disease passes.

The two developmental phases of pulmonary tuberculosis which can be identified clinically are linked by important microscopic changes which escape detection by methods now available for examining living patients. These changes occur during periods of variable length when the disease seems to be quiescent, but it is not until lesions sufficiently large to cast shadows on roentgenograms are produced that the beginning of the second phase of the development of pulmonary tuberculosis can be recognized.

Chronic Pulmonary Tuberculosis of the Adult Type.—Details concerning the children in whom chronic pulmonary tuberculosis either existed at the initial examination or developed during the course of the follow-up study are provided by tables 5 and 6.

Of the 5,747 children who were traced and whose reaction to the initial tuberculin tests were negative, 16 acquired chronic pulmonary tuberculosis of the adult type. Twelve of these 16 patients were not reexamined at Lymanhurst between the time of their entry to the clinic

and the date of the discovery of their pulmonary disease (table 5, group A). The average interval between these two examinations was nine years. Detailed information relative to the train of events which culminated in the pulmonary tuberculosis detected in this group of 12 children when they had attained an average age of 20 years is not available. Subsequent to the discovery of the presence of chronic pulmonary tuberculosis, these patients were traced for an additional average period of two and six-tenths years, during which 5 children, or 41.7 per cent of the group, died of the disease.

TABLE 5.—*Data on Acquired Chronic Pulmonary Tuberculosis in Children with Initial Negative Tuberculin Reactions*

Group A							
						Incidence of Chronic Pulmonary Tuberculosis in 5,747 Traced Children	
Number of Children	Average Age When Tuberculin Reaction Was Last Negative, Yr.	Subsequent Interval With No Reexaminations, Yr.	Average Age When Pulmonary Tuberculosis Was Discovered, Yr.	Average Age at Time of Last Examination	Number and per Cent Dead from Tuberculosis	Per 1,000 Children	Per 1,000 Person Years of Follow-up Experience
12	11.7	9.0	20.7	23.3	5 (41.7%)	2.1	0.34

Group B							
						Incidence of Chronic Pulmonary Tuberculosis in 5,747 Traced Children	
Number of Children	Average Age When Tuberculin Reaction Was Last Negative	Average Age When Tuberculin Reaction Was First Known to be Positive	Average Age When Chronic Pulmonary Tuberculosis Was Discovered	Average Age at Time of Last Examination	Number and Per Cent Dead from Tuberculosis	Per 1,000 Children	Per 1,000 Person Years of Follow-up Experience
4*	10.3	13.3	17.8	20.5	0	0.7	0.11

* In the lungs of 1 additional child a small subapical infiltration has been present for several months. Diagnosis is pending.

The remaining 4 children who entered Lymanhurst with negative reactions to tuberculin but in whom chronic pulmonary tuberculosis later developed (table 5, group B) were found to have acquired sensitivity to tuberculin at an average age of 13.3 years, or three years subsequent to the time their reactions were last known to be negative. Pulmonary tuberculosis made its appearance in these 4 patients four and a half years after the transition from the uninfected to the infected state was demonstrated. During the two and seven-tenths years that have elapsed since this form of the disease was detected none of the patients has died.

The presence at the time of the first examination of chronic pulmonary tuberculosis in 49 members of the series of 2,467 infected children who were traced has already been mentioned (table 6, group A). When the disease was detected in these patients they had an average

age of 13.4 years. They were traced for an additional seven and four-tenths years, during which 14 children, or 28.6 per cent of the group, died of the disease.

The remaining 2,418 members of the infected patients who were traced presented no evidence of chronic pulmonary tuberculosis when they entered the clinic. During the course of the follow-up study this form of the disease was acquired by 58 members of the group (table 6, group B). These 58 patients had an average age of 11.6 years when their reactions to tuberculin were first known to be positive, and they had attained a mean age of 16.5 years before the presence of chronic pulmonary tuberculosis was detected. They were traced for an addi-

TABLE 6.—*Data on Acquired Chronic Pulmonary Tuberculosis in Children with Initial Positive Tuberculin Reactions*

Group A			
Number of Children	Average Age When Pulmonary Tuberculosis Was First Found	Last Known Age	Number and per Cent Dead
49	13.4	20.8	14 (28.6)

Group B						
					Incidence of Chronic Pulmonary Tuberculosis	
Number of Children	Age When Positive Tuberculin Reaction Was Found	Age When Chronic Pulmonary Tuberculosis Was Found	Last Known Age	Number and per Cent Dead	Per 1,000 Children	Per 1,000 Person Years of Follow-up Experience
58*	11.6	16.5	21.8	18 (31.0%)	24.0	3.4

* Twenty-one additional children have acquired small pulmonary lesions which have persisted over a period of months, but diagnosis is still pending.

tional average period of five and three-tenths years, during which 18 patients, or 31 per cent of the group, died of tuberculosis.

The initial and follow-up examinations of the children at Lymanhurst included in this study revealed a total of 123 patients with chronic pulmonary tuberculosis at an average group age of 15.7 years (combined data of tables 5 and 6). These patients were traced for an additional average period of five and eight-tenths years, during which 37 patients, or 30.1 per cent of the group, died of the disease. These results, obtained in a group of children who received the benefit of various therapeutic procedures, disclose the seriousness of the second phase of the evolution of pulmonary tuberculosis.

Miliary tuberculosis, tuberculous meningitis and tuberculosis in the bones and joints comprised the additional clinically important forms of the disease which appeared in the children whose records form the basis of this report.

Miliary tuberculosis and tuberculous meningitis developed in 10 members of the group who entered the clinic with positive reactions to tuberculin, whereas osteoarticular disease was acquired by 22 members of this group and by 3 members of the group whose reactions to initial tuberculin tests were negative. During the course of the follow-up study clinically serious forms of tuberculosis (all chronic pulmonary and miliary disease, tuberculous meningitis and osteoarticular tuberculosis combined) were acquired, therefore, by a total of 19 members of the original uninfected group and by 90 members of the infected group.

The combined incidence of these four serious varieties of tuberculosis per thousand traced children amounted to 3.3 cases for the orginal uninfected group and 37.2 cases for the infected group, whereas their incidence per thousand person years of follow-up experience was 0.54 cases for the former and 5.29 cases for the latter series of patients. The rates at which these grave forms of tuberculosis were acquired by the traced patients who entered Lymanhurst with positive reactions to tuberculin were approximately tenfold the rates observed for the children entering with negative reactions.

SUMMARY

Initial Examination.—An analysis of the records of 10,003 children with an average age of 9 years is presented.

Initial reactions to tuberculin were negative for 7,107 of these children and positive for the remaining 2,896.

On entry to the clinic roentgenograms of the chest were made of 84.3 per cent of the uninfected children and of 95.5 per cent of the infected patients.

The percentage of children whose lungs were interpreted as normal on the basis of initial roentgenograms amounted to 92.9 for those with negative reactions to tuberculin and 57 for the tuberculin-sensitive group.

Roentgenographically demonstrable lesions which were considered nontuberculous were revealed by 4.3 per cent of the roentgenograms of the children with negative reactions to tuberculin and by 4.7 per cent of the roentgenograms of the infected children. In each series of patients the incidence of lesions of this character tended in general to increase gradually in successive age groups.

All of the remaining lesions reported by the roentgenologist for these two series of children were of the type which the tubercle bacillus produces.

Relatively benign pneumonic infiltrations deemed representative of the earliest roentgenographically demonstrable stage of the broad primary phase of the evolution of pulmonary tuberculosis were found in 166 members of the infected group. The incidence of such lesions reached a maximum at about the third year of life and then diminished. Primary

pneumonic tuberculous infiltrations were found only in the tuberculin-sensitive group. A general tendency for these lesions first to persist and later to resolve slowly was noted.

Calcified and fibrosed deposits were revealed by 2.8 per cent of the initial roentgenograms of the children with negative reactions to tuberculin. The incidence of these lesions tended to increase slightly with advancing age.

Calcified and fibrosed deposits were disclosed by 30.6 per cent of the initial roentgenograms of the infected children. For this series of patients the incidence of these lesions increased rapidly until the age of 8.5 years but subsequently manifested no consistent change. The calcified and fibrosed deposits were considered as representing an older stage in the evolution of primary pulmonary tuberculosis than was represented by the pneumonic tuberculous infiltrations found in 166 members of the series of infected patients.

Initial roentgen study of 2,767 tuberculous children disclosed 49 patients with chronic pulmonary tuberculosis of the adult type. This form of the disease made its first appearance at the seventh year of life and tended to increase in relative frequency in each successive age group.

Follow-Up Study.—Follow-up data derived either from repeated roentgen studies, repeated tuberculin tests or verbal inquiry were obtained for 80.9 per cent of the children with negative reactions to tuberculin and for 85.2 per cent of the infected group.

Approximately 72 per cent of each group of patients who were traced received the type of reexamination deemed necessary to disclose the presence or absence of clinical tuberculosis (repeated roentgen examinations for the infected children and repeated roentgen studies or repeated tuberculin tests for the uninfected children).

The average initial age of the patients who were traced amounted to 8.4 years for the uninfected group and 9.9 years for the infected group. The former were traced for an average of six and one-tenth years and the latter for six and nine-tenths years. The total person years of follow-up experience amounted to approximately 35,000 years for the uninfected group and 17,000 years for the infected group.

During the course of the follow-up study chronic pulmonary tuberculosis was acquired by 16 of the 5,747 traced children whose initial tuberculin reactions were negative. For this group the incidence of this clinical variety of tuberculosis amounted to 2.8 cases per thousand children and 0.46 cases per thousand person years of follow-up experience.

Of the 2,467 traced children who entered Lymanhurst with positive reactions to tuberculin, 2,418 presented no evidence of chronic pulmonary tuberculosis at the time of the first examination. During the

course of the follow-up study this form of the disease was acquired by 58 members of the group. The incidence of newly developed examples of chronic pulmonary tuberculosis observed for this group of 2,418 infected children amounted to 24 cases per thousand patients and 3.4 cases per thousand person years of follow-up experience.

Follow-Up Roentgenographic Study.—Follow-up roentgen examination extending throughout an average period of seven years of 2,670 children with negative reactions to tuberculin and of 1,784 tuberculin-sensitive children disclosed marked changes in roentgenographic findings chiefly for the infected group, in which the incidence of roentgenographically normal lungs decreased from 53.9 to 36.9 per cent.

During the follow-up roentgen study of the infected patients the incidence of primary pneumonic tuberculous infiltrations decreased from an average of 7.9 per cent to one of 0.7 per cent. This change resulted from the spontaneous resolution which these lesions were observed to undergo.

The incidence of calcified and fibrosed deposits changed from an initial 31.6 per cent to a final 53.1 per cent. A major portion of this change resulted from the appearance of lesions of this character in many of the infected children whose initial roentgenograms revealed no evidence of pathologic conditions.

During the course of the follow-up roentgen study the incidence of chronic pulmonary tuberculosis increased from 2.7 to 6 per cent in the infected group.

During the course of the follow-up study serious forms of tuberculosis which I consider representative of the second clinically demonstrable phase of the evolution of the disease (chronic pulmonary and miliary disease, tuberculous meningitis and osteoarticular tuberculosis combined) were acquired by 19 members of the originally uninfected group and by 98 members of the infected group.

The combined incidence of these four serious varieties of tuberculosis per thousand patients and per thousand person years of follow-up experience observed for the infected group was approximately tenfold that recorded for the children who entered Lymanhurst with negative tuberculin reactions.

CONCLUSIONS

1. The complex immunologic changes which infections with virulent tubercle bacilli produce do not provide a solution for the problem of human tuberculosis.

2. Infections with this organism serve to perpetuate tuberculosis in successive generations of man.

3. The eradication of tuberculosis is contingent on the prevention of infections with virulent tubercle bacilli.

INTERCHANGEABILITY OF ZINC CRYSTALLINE INSULIN AND AMORPHOUS INSULIN

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In a former publication,[1] the need for standardized and well established control of diabetes mellitus in the child was emphasized, not only for the management of the disease but also as a prerequisite for studies concerned with the relative efficacy of varied forms of treatment. It was stated that children with diabetes mellitus showed no consistent qualitative or quantitative difference in response to zinc crystalline insulin and to the amorphous product now commonly used. This report presents a summary of the data which served as a basis for that conclusion.

Subjects used for study were limited to diabetic children whose cases satisfied the following criteria:

1. Prolonged preliminary observation during which the insulin requirement had become constant for the standard conditions imposed by the therapeutic regimen.

2. Maintained aglycosuria and freedom from clinically significant insulin shocks.

3. Approximately normal diurnal blood sugar fluctuations from day to day.

Blood sugar samples were obtained once or twice each week at the following hours: 6 a. m., 7 a. m., 9 a. m., 11 a. m., 4 p. m., 10 p. m., 3 a. m. and 6 a. m. A micromodification of the Folin-Wu method was used for estimation of sugar content; the Somogyi method of precipitation was employed. Insulin was administered at 6:30 a. m., 11 a. m. and 4:30 p. m. and once during the night (at 10, 12 or 2 o'clock). The total day's dose was distributed among the four injections with a percentage distribution of approximately 35, 22, 28 and 15.

From the Department of Pediatrics, College of Medicine, State University of Iowa.

1. Jackson, R. L., and Boyd, J. D.: Stabilization of the Diabetic Child, J. A. M. A. **112**:1017 (March 11) 1939; Am. J. Dis. Child. **59**:332 (Feb.) 1940.

The constancy of response which may be attained with the therapeutic regimen used for these children is illustrated in chart 1. This chart shows the mean blood sugar levels and the diurnal fluctuations observed with 31 diabetic patients as contrasted with the range observed with nondiabetic children. The values reported in table 1 show the degree of oscillation and the type of blood sugar level encountered in these 31 standardized subjects. The data include an aggregate of 906 blood sugar estimations made during six hundred and eleven days of study. The data prove the practicability of maintaining approximately normal blood sugar levels in the diabetic child.

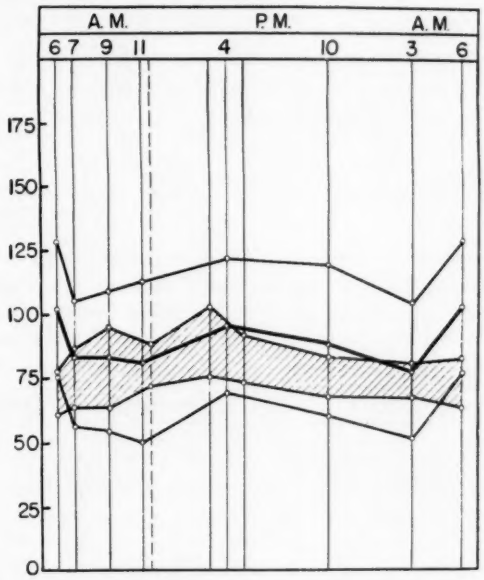

Chart 1.—Diurnal blood sugar fluctuation of normal children as contrasted with that of well stabilized diabetic children. The cross-hatched area represents the gross range observed in examination of nondiabetic children; the dark line represents the average; the other two curves bound the range included by two standard deviations of the children with diabetes mellitus. Each group was under the same dietary regimen; the children with diabetes received insulin.

The relative efficacy of zinc crystalline insulin and amorphous insulin was studied with 14 of these children. Each subject had been under careful hospital management for several weeks preceding stabilization. The constancy of the diabetic status was confirmed by continuation of the hospital management for a period averaging fifteen days, during which time the comparative study was made. The types of insulin studied were alternated at intervals of approximately a week. No other changes in the regimen were permitted. The average blood sugar levels observed

when either zinc crystalline insulin or amorphous insulin was used, with corresponding standard deviations, standard errors and critical ratios, are shown in table 2. The ratios between the respective standard errors and standard deviations establish the constancy of the data; the possibility of error due to chance sampling is less than 1 : 500 in any instance.

A comparison of corresponding blood sugar values shows that no statistically significant difference is demonstrable between the results

TABLE 1.—*Diurnal Blood Sugar Levels of Thirty-One Stabilized Diabetic Children After Administration of Amorphous or Zinc Crystalline Insulin*

Hour	Number of Determinations	Mean	Standard Deviation	Standard Error
6 a. m.	114	101	26	2.4
7 a. m.	114	81	24	2.3
9 a. m.	112	81	26	2.5
11 a. m.	111	79	27	2.5
4 p. m.	114	96	27	2.5
10 p m.	114	90	31	2.9
3 a. m.	113	77	26	2.4
6 a. m.	111	102	23	2.6

TABLE 2.—*Comparison of Mean Diurnal Blood Sugar Levels Observed After Administration of Amorphous Insulin With Those Observed After Administration of Zinc Crystalline Insulin* *

	Lilly's Insulin (6 Patients)							Stearns' Insulin (8 Patients)						
	Amorphous (A)			Crystalline (C)				Amorphous (A′)			Crystalline (C′)			
Hour	Mean	Standard Deviation	Standard Error	Mean	Standard Deviation	Standard Error	Critical Ratio,† A & C	Mean	Standard Deviation	Standard Error	Mean	Standard Deviation	Standard Error	Critical Ratio,† A′ & C′
6 a. m.	100	21	6.5	94	23	6.9	0.63	109	18	5.7	95	14	4.3	1.80
7 a. m.	73	18	5.3	67	15	4.6	0.86	84	30	9.4	88	24	7.7	0.33
9 a. m.	74	22	6.5	86	26	8.4	1.13	81	22	7.1	89	33	10.9	0.61
11 a. m.	86	27	8.6	96	28	8.4	0.81	66	18	5.7	61	14	4.2	0.70
4 p. m.	97	22	7.1	94	25	7.4	0.33	92	13	4.3	97	15	4.6	0.79
10 p. m.	91	35	10.4	91	32	9.6	0	104	31	10.1	81	23	8.8	1.71
3 a. m.	83	25	7.4	77	30	9.1	0.53	66	18	5.8	64	23	7.6	0.20
6 a. m.	95	26	7.9	94	27	8.0	0.09	102	13	4.2	96	10	3.1	1.14

* Values of less than 3 are not considered statistically significant.

† The critical ratio is obtained through the formula $CR = \frac{\sigma_1 - \sigma_2}{\sqrt{\sigma^2(\sigma_1) + \sigma^2(\sigma_2)}}$

obtained with amorphous insulin and those obtained with zinc crystalline insulin as supplied through two commerical sources. This is evidenced by the critical ratio, listed in the right hand column. Such differences as are present are explainable on the basis of chance and are no greater than those observable within the data pertaining to either group alone. The similarity of response with the two forms of insulin from two commercial sources is shown graphically in chart 2.

One would predict no noteworthy difference in response to various brands of insulin, as each is produced under controlled conditions imposed by licensure of the manufacturer. Further studies have been made with amorphous and with zinc crystalline insulin available from the other licensees. The limited volume of data does not justify statistical evaluation, but the values do not indicate any real difference between the effect of one form of insulin and that of another or between the products of different manufacturers.

The purported increase in efficacy and in prolongation of effect of insulin in the form of zinc crystals as contrasted with insulin in the amorphous form which has been described by some observers may be explained by the fact that human subjects who had not reached full

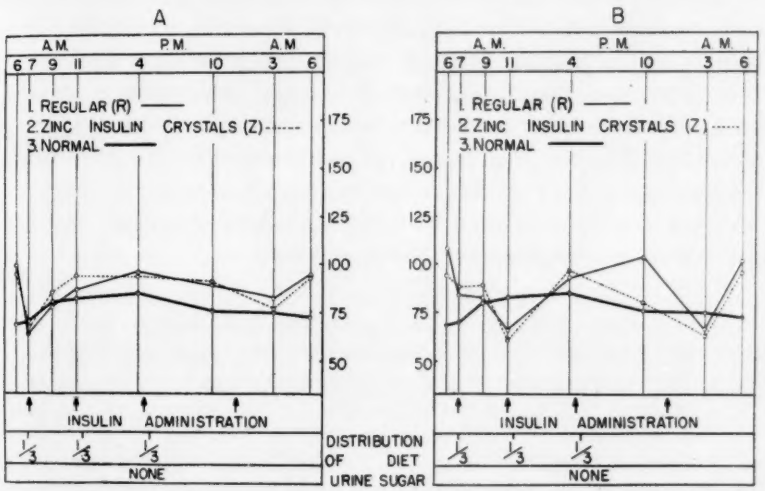

Chart 2.—Average diurnal blood sugar fluctuations of well stabilized diabetic children receiving equivalent units of amorphous insulin (R) and the zinc crystalline insulin (Z), other factors being constant. In each instance the regimen and response had been constant for several days before blood sugar values were accepted for inclusion (based on an aggregate of two hundred and seven hospital days and 336 determinations of blood sugar). The heavy line in each chart indicates average blood sugar values obtained in observations on nondiabetic children under similar dietary regimen (chart 1). The charts show the values obtained in observations. *A,* on 6 diabetic children given Lilly's amorphous (R) as compared with Lilly's crystalline (Z) insulin; *B,* on 8 diabetic children given Stearns' amorphous (R) as compared with Stearns' crystalline insulin (Z).

stability of response were used. Conclusions drawn from such studies seem unreliable.

From the evidence offered, it is concluded that no distinction need be made between the qualitative or quantitative effects of doses of equal unitage of zinc crystalline and of amorphous insulin, or between the effects of corresponding products of various manufacturers.

PROBABLE MECHANISM OF THE "PHYSIOLOGIC" HYPOPROTHROMBINEMIA OF THE NEWBORN

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The human newborn infant has hypoprothrombinemia in a moderate degree at birth,[1] in greater degree between the second and the sixth day of life [2] and in gradually diminishing degree throughout the first twelve months of life.[1] The causes for this deficiency remain obscure. This hypoprothrombinemia, which renders the newborn infant susceptible to profuse loss of blood, has been attributed to a possible dietetic deficiency in the mother, though plasma prothrombin values in the mother at term are usually higher than normal.[3] The condition develops too early in the newborn infant to be attributable to a food deficiency in the child. The lack of a well developed bacterial flora in the intestine has been suggested as another cause.[2a]

A rare anomaly observed in a full term mulatto infant cast light unexpectedly on the mechanism of this deficiency.

On the second day of life the infant became intensely jaundiced and vomited blood and all food administered; nothing but meconium was passed by bowel. For the next nine days there was little change. The serum icterus index was 150 units; the plasma prothrombin [4] content was less than 1 per cent of normal, and skin punctures bled for several hours. The plasma fibrinogen and the number of platelets were normal. Intramuscularly injected blood and dextrose administered by hypodermoclysis helped to keep the infant alive. On the eleventh day of life the jaundice began to clear up; a small, bile-tinged stool was passed; the bilirubin content of the serum dropped to 2.6 mg. per hundred cubic centimeters; the plasma prothrombin content rose to 113 per cent of normal, and all manifestations of bleeding ceased. The infant continued, however, to vomit all that was placed in his stomach by tube, and died.

Autopsy on the seventeenth day after birth revealed: a septum completely separating the first from the middle portion of the duodenum; a patent, functioning biliary tract with the common duct opening just distally to the septum, and a collapsed small and large intestine holding a small amount of bile-stained debris.

From the Division of Hematology, Department of Medicine, Jefferson Medical College and Hospital.

1. Owen, C. A.; Hoffman, G. R.; Ziffren, S. E., and Smith, H. P.: Proc. Soc. Exper. Biol. & Med. **41**:181, 1939.

2. (*a*) Quick, A. J., and Grossman, A. N.: Proc. Soc. Exper. Biol. & Med. **41**:227, 1939. (*b*) Owen and others.[1]

3. Norris, R., and Rush, A.: Personal communication to the author.

4. Quick, A. J.; Stanley-Brown, M., and Bancroft, F. W.: Am. J. M. Sc. **190**:501, 1935.

The atresia of the duodenum made it impossible (1) for the food to pass down the intestine and be absorbed; (2) for the food to be mixed with the bile so that fat digestion and proper utilization and absorption of vitamin K could take place, and (3) for bacterial contamination of the bowel to occur, with consequent synthesis of vitamin K.[5]

The return of the plasma prothrombin level to normal and the cessation of the hemorrhagic tendency cannot therefore be ascribed to the operation of factors connected with the ingestion, digestion and absorption of substances essential for prothrombin formation or with the synthesis of vitamin K by bacterial action. The improvement coincided in time with the diminution in the bilirubinemia and with the establishment of adequate bile flow, while the intestinal obstructive factors continued to operate.

Icterus gravis such as this infant had is regarded as an exaggeration of the "physiologic" icterus observed in the majority of newborn infants.[6] Likewise the extreme hypoprothrombinemia of this child may be regarded as an exaggeration of the "physiologic" hypoprothrombinemia of the newborn. The simultaneous development and disappearance of these two anomalies under the circumstances just described suggests that they may have a common cause, namely, the known functional insufficiency of the liver of the newborn infant, as partially manifested by its reduced capacity for excretion of bilirubin or dye and by its reaction to tests of other functions.[7]

Further points in support of this view are: 1. The hypoprothrombinemia corresponds approximately in time of onset, in severity and in duration to the newborn infant's "physiologic" hyperbilirubinemia and jaundice, the latter of which begins about the second day of life, reaches its peak about the fifth and begins to disappear by the seventh day. 2. Infants with hemorrhagic disease almost always have icterus or a hyperbilirubinemia, while, conversely, in icterus gravis or the icterus resulting from congenital atresia of the bile ducts, a tendency to hemorrhage is prominent. 3. The liver plays an important role in the formation of prothrombin, partial removal of the liver resulting in a marked decrease in the plasma prothrombin[8] and injuries to the liver in adults (chloroform and phosphorus poisoning, complete or incomplete biliary obstruction with regurgitation jaundice) being accompanied by marked decreases in the plasma prothrombin and by the appearance of a hemorrhagic tendency.[9]

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5. Almquist, H. J., and Stokstad, E. L. R.: J. Nutrition **12**:329, 1936.
6. Yllpo, A.: Ztschr. f. Kinderh. **17**:334, 1918.
7. Snelling, C. E.: J. Pediat. **2**:329, 1933.
8. Warner, E. D.: J. Exper. Med. **68**:831, 1938.
9. (*a*) Smith, H. P., and Brinkhous, K. M.: Am. J. Physiol. **114**:667, 1936. (*b*) Quick and others.[4] (*c*) Butt, H. R.; Snell, A. M., and Osterberg, A. E.: Proc. Staff Meet., Mayo Clin. **13**:74, 1938.

The "physiologic" icterus of the newborn results from the fact that an excessive amount of bilirubin derived from hemolysis of erythrocytes is delivered for excretion to a liver with a subnormal excretory capacity.[10] It is perhaps during this interval when a condition of hyperbilirubinemia is making great demands on a defective bilirubin excretory mechanism that a period of hepatic insufficiency more pronounced than that already present in the newborn supervenes, as well as further impairment in the formation of prothrombin. The functional and structural immaturity of the liver of the newborn child probably accounts for the fact that a prothrombin deficiency appears—in comparison with the time of its appearance in the adult liver—relatively early, after a short period of incapacitation. It follows that any measures designed to reduce the incidence and severity of "physiologic" icterus, such as prompt tying of the cord after birth,[11] or measures known to overcome the hypoprothrombinemia of obstructive jaundice of adults, such as vitamin K and bile therapy,[9c] may have a corresponding beneficial effect on the hypoprothrombinemia of the newborn.

NOTE.—Since this paper was submitted Norris and Bennett[12] have observed that the blood coming from the placenta has about 10 per cent more prothrombin than that entering it from the baby, an indication, perhaps, that the placenta is engaged in the production of prothrombin up to the time of birth. Prothrombin is associated chiefly with the globulin fraction of the plasma, and the plasma globulins are thought to be made in the placenta and not obtained from the mother as is albumin.[13] A globulin substance resembling prothrombin in some of its characteristics has been extracted from the placenta by Eley and his co-workers.[14] If the placenta proves to be the infant's chief source of prothrombin before birth, then separation of the infant from that organ at birth throws on a functionally and structurally immature liver the immediate task of making prothrombin. This fact added to those already presented may result in a lowered plasma prothrombin content during the first days of life.

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10. Rich, A. R.: Bull. Johns Hopkins Hosp. **47**:238, 1930.
11. Book, N.: Canad. M. A. J. **33**:269, 1935.
12. Norris, R., and Bennett: Personal communication to the author.
13. Darrow, D. C., and Carey, M. K.: J. Pediat. **3**:573, 1933.
14. Eley, R. C.; Green, A. A., and McKhann, C. F.: J. Pediat. **8**:135, 1936

Case Reports

TREATMENT OF RITTER'S DISEASE WITH SULFAPYRIDINE

REPORT OF A CASE WITH RECOVERY

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That serious and rather rare disease of the skin which Gottfried Ritter von Rittershain [1] first studied in 1868 and described some ten years later continues to remain a subject of much controversy.[2] Briefly, this disease occurs in early infancy, either sporadically or epidemically, and is characterized by rapidly spreading redness, vesicles and bullae, together with epidermolysis and exfoliation. The epidermolysis is probably the most characteristic finding.[2a] It is manifested as the peeling away of the uninvolved skin on the slightest rubbing or other trauma and the leaving of a raw, oozing surface. When the disease is mild this may be found around the bullae, and when the condition is severe, it may be found anywhere over the uninvolved skin. Figures for mortality vary. From his studies, which, incidentally, represent the largest series, Ritter von Rittershain [1a] reported a mortality of 50 per cent. Finkelstein [3] reported a mortality of 60 to 70 per cent. Carl Leiner [2a] wrote of approximately 20 cases observed in twenty years, with recovery in only 2. Griffith and Mitchell [4] reported a mortality of 50 per cent. It is difficult to get figures for mortality at present, since the disease is so uncommon that most physicians have never seen a case and only single or several cases are reported in the present literature. Of 4 patients previously observed by one of us (L. G.), 3 of whom were in this city, not a single one recovered.

From the Children's Hospital.

1. Ritter von Rittershain, G.: (*a*) Die exfoliative Dermatitis jüngerer Säuglinge, Centr.-ztg. f. Kinderh. **2:3, 1878**; (*b*) Die exfoliative Dermatitis jüngerer Säuglinge und Cazenave's Pemphigus foliaceus, Arch. f. Kinderh. **1:53, 1880.**

2. (*a*) Leiner, C.: Dermatitis exfoliativa Neonatorum (Pemphigus malignus), in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1930, vol. 14, pt. 1. (*b*) Neff, F. C.: Dermatitis Exfoliativa Neonatorum, Arch. Pediat. **51:465, 1934.**

3. Finkelstein, cited by Leiner.[2a]

4. Griffith, J. P. C., and Mitchell, A. G.: The Diseases of Infants and Children, ed. 2, Philadelphia, W. B. Saunders Company, 1937, p. 1101.

There is no definite treatment for the condition. In addition to the usual kinds of local therapy, many methods have been suggested, from dietary changes to ultraviolet radiation [2b] and transfusions.[4] According to reports, the prognosis depends, in short, on the extent of the lesions, whether the phenomenon of epidermolysis is found only in the neighborhood of the bullae or elsewhere on the skin, whether the case is a sporadic one or occurred during an epidemic and whether there are such complications as infection of the umbilicus with peritonitis, septicemia and pneumonia.

The etiology of Ritter's disease is still obscure, and it is not proposed here to enter into a discussion of this phase.[5] Most authors are agreed that the disease is an infection, probably pyogenic in nature, with Staphylococcus aureus implicated most frequently. The exogenous infection is thought to be associated with septicemia, although few positive cultures of the blood have been reported and no organisms have been reported in the viscera in the few available postmortem studies. From the experiences of one of us (L. G.) with contact infection in Ritter's disease, we believe essentially with Zakon [6] in the relation of at least some types of Ritter's disease to impetigo bullosa of adults. There are others who insist that Ritter's disease is merely a symptom complex which may result from any number of different diseases. Because of the continued rarity of the disease, it seems advisable to report, with qualifications, even this single case.

REPORT OF CASE

P. W., a girl 4 weeks old, was first seen at the age of 3 weeks, suffering from mild gastroenteritis. She weighed 7 pounds 8 ounces (3,402 Gm.), having lost ½ pound (227 Gm.) during the previous week. Examination revealed nothing besides moderate malnutrition and slight pallor. The skin was normal except for excoriation of the buttocks, which had appeared with the onset of the gastroenteritis. There was no suspicion of impetiginization.

The family history was unremarkable except that one sibling had suffered from severe infantile eczema throughout the first year of its life. There was no history of contact with impetigo or other cutaneous infection.

Symptomatic treatment was ordered for the gastroenteritis, and exposure to air plus applications of starch U. S. P. (corn starch) were recommended for the skin.

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5. Darier, J.: Précis de dermatologie, Paris, Masson & Cie, 1928. Weidman, F., and Gilman, R. L.: Pathologisch-anatomische Veränderungen bei allgemeiner Exfoliation der Haut bei Neugeborenen mit besonderer Berücksichtigung der Ritterschen Krankheit, Arch. f. Dermat. u. Syph. **167**:491, 1933. Griffith and Mitchell.[4]

6. Zakon, S. J.: The Relationship of Dermatitis Exfoliativa Neonatorum Ritter and Impetigo Bullosa in the Adult, Arch. Dermat. & Syph. **24**:830 (Nov.) 1931.

When the infant was seen again one week later, the intestinal condition had improved, but a severe cutaneous eruption had developed, which had apparently started on the scalp and face and within twenty-four hours had spread over the trunk and the perineum.

The infant appeared severely ill. The general inspection suggested that she had been scalded. The rectal temperature was 101.5 F.; the pulse rate was 100, and the respiratory rate, 35. There was a generalized cutaneous eruption involving especially the scalp, the face, the upper part of the trunk and the perineal area. The lesions consisted of raw oozing surfaces limited by shreds of overhanging whitish and reddish skin. Scattered in the areas of apparently uninvolved skin were small vesicles and bullae with definite inflammatory areolas, several of which were suggestive of typical impetigo. Fissured lesions were found about the mouth and anus. The lesions were spotty over the back, but the large oozing red areas and the bullae were found on both flanks. The abdomen and the lower part of the thorax anteriorly were relatively little involved. In a few areas

Appearance of the skin of a patient with Ritter's disease forty-eight hours after institution of treatment with sulfapyridine. The large "burnlike" area is still present. The small vesicles and bullae are healing. The phenomenon of epidermolysis is everywhere absent from the skin at this time.

in this region there were whitish soft lesions underneath the skin. These gave the impression of air pockets. The phenomenon of epidermolysis was easily obtained in this area with the slightest amount of friction from a tongue depressor or a gloved finger. There were no lesions of the mucous membranes.

In addition to these conditions, the general physical examination revealed bilateral purulent otitis media, which appeared forty-eight hours after hospitalization of the patient. Immediate paracentesis was performed. A smear or culture of the fluid was not obtained.

Examination of the urine showed no pathologic conditions. There were 4,600,000 red blood cells and 10,300 white blood cells. The differential count revealed 25 per cent polymorphonuclear leukocytes, 53 per cent lymphocytes, 11 per cent large mononuclears, 10 per cent eosinophils and 1 per cent transitionals. The Wassermann test of the blood was negative. Culture of old but still active cutaneous

lesions yielded Streptococcus viridans, Staph. aureus (hemolytic type), a gram-negative rod belonging to the Citrobacter group and a sporing rod.[7]

Dark field examination of the cutaneous lesions gave results negative for spirochetes. The high percentage of eosinophils present is unusual for Ritter's disease, although it is not uncommon in many generalized dermatoses.

General treatment consisted of daily blood transfusions (amount, 50 cc.) and administration of sulfapyridine. The sulfapyridine was given in an initial dose of 6 grains (0.39 Gm.), followed by 2 grains (0.13 Gm.) every four hours for the first three days, then 1 grain (0.06 Gm.) every six hours for four days, at which time the treatment was stopped because of improvement in the patient's condition. The sulfapyridine level in the blood reached 11.7 mg. per hundred cubic centimeters after twenty-four hours. On the fourth day it dropped to 5.4 mg. After the dose was decreased the level was not checked. The use of sulfapyridine was continued for several days after the eruption had almost entirely cleared, because a relapse occasionally occurs in cases of Ritter's disease.

Locally, an ointment containing 2.5 per cent ammoniated mercury was applied to the face and scalp, starch to the body and tincture of benzoin to the buttocks and the perineal region.

Within thirty-six to forty-eight hours after admission the patient showed great improvement (fig. 1). The skin began to lose its fiery red color, and most of the surfaces began to dry out. Desquamation ceased, and the phenomenon of epidermolysis could no longer be elicited.

The fever present on the patient's admission to the hospital disappeared within four days, probably owing to the coincidental improvement in the otitis media, as fever is supposedly rare in cases of uncomplicated Ritter's disease. The subsequent course was one of steady improvement, and the patient was dismissed from the hospital on the sixteenth day. The skin was normal, the ears were well and there had been a gain in weight of 1½ pounds (680 Gm.).

COMMENT

There was no doubt about the diagnosis in this case. Syphilis was ruled out by the laboratory data and by the course of the illness. Severe drug eruption was ruled out by the appearance and the course and also by the fact that the use of drugs was continued long into the stage of regeneration of the skin. Although the lesions in this case began in the face, involvement of the forehead and scalp is uncommon, according to the literature. It is interesting, also, to emphasize here that this is a sporadic case and occurred in the home and that there was no evident source of contact with impetigo. According to the meager details of the early history obtained from the parents, there may have been typical impetigo spots before the rapid extension began. Certainly at the time of the examination areas of impetigo could still be seen. From the extent of the lesions which eventually developed, the condition in this case could be considered as a severe form of Ritter's disease. The culture obtained from the skin did not offer anything of value. Cultures of the blood and inoculation of animals, which have been suggested by

7. Lilly Glesne was the bacteriologist.

several investigators, were not done. The otitis media began apparently after the development of the cutaneous eruption, and the paracentesis had no effect on the lesions, although it did have some effect on the temperature. In the early part of the illness there were no lesions in the auditory meatuses. Later, the sign of epidermolysis was obtained in the ear also. This was noted especially when any cleansing of the ears was done. It is difficult to estimate the effect of the sulfapyridine on the otitis media, since paracentesis was done and administration of sulfapyridine started at approximately the same time. Fever, apparently, is not a constant condition in cases of uncomplicated Ritter's disease. Another point of clinical interest is the fact that even before the disease had entirely cleared the phenomenon of epidermolysis could not be obtained, in the neighborhood of the large reddened areas or elsewhere. From doubtful historical data alone, the disease apparently began as impetigo.

To try to analyze the effect of treatment in this case one must first dismiss the importance of the local treatment. Since this child had different forms of local medication in different areas of the body and had no antiseptics of any kind across the trunk, where the lesions later became extensive, and since all the lesions cleared with apparently the same rapidity, the improvement in the infant's skin was due to the general treatment. One of us (L. G.) has observed the effect of transfusions in a few cases, in which they were without result. Chemotherapy was suggested in this case because of the evidence that the disease was probably the result of infection. In the bacteriologic studies of Ritter's disease available, the staphylococcus has been considered more frequently than other organisms. There are a few controversial reports in the literature on the value of sulfanilamide in the treatment of staphylococcic diseases of the skin. Marcus [8] insisted it has no value in the treatment of impetigo. Fenton and Hodgkiss [9] have reported recovery of a patient with septicemia due to Staph. aureus after treatment with sulfapyridine. In their recent review of sulfanilamide, Bigler and Haralambie [10] asserted: "So far the reports on the use of sulfanilamide against staphylococcic infections have not been encouraging."

Administration of sulfapyridine was started in this case, together with blood transfusions, some four days after the onset of the extension of the disease. This is approximately shortly before the height of the illness in the average case of Ritter's disease. Improvement was detected

8. Marcus, M.: Sulphanilamide in Staphylococcal Skin Infections, Brit. M. J. **2**:92, 1938.

9. Fenton, W. J., and Hodgkiss, F.: Staphylococcal Septicaemia Treated by M. & B. 693, Lancet **2**:667, 1938.

10. Bigler, J. A., and Haralambie, J. Q.: Sulfanilamide and Related Compounds: A Review of the Literature, Am. J. Dis. Child. **57**:1110 (May) 1939.

for the first time, within thirty-six to forty-eight hours after the start of the new systemic treatment, by the failure to elicit any sign of epidermolysis. The improvement was rapid. The child had a total of 58 grains (3.75 Gm.) of sulfapyridine. We do not know whether it is absolutely necessary to obtain as high an initial level of sulfapyridine in the blood (11.7 mg. per hundred cubic centimeters) as we did. In spite of the definite cutaneous reaction there was no apparent toxicity from the sulfapyridine. Similar extensive bullous eruptions, such as pemphigus, also show no predisposition toward toxic reactions from the sulfanilamide compounds. In the period of observation that has followed there has been no relapse or recurrence of lesions. Likewise, there have been no lesions in other members of the family.

CONCLUSIONS

Although it is hazardous to draw conclusions from a single case, it can be stated that in a case of severe sporadic Ritter's disease improvement and rapid cure were associated with general treatment consisting of transfusions and administration of sulfapyridine. The true value of sulfapyridine in the treatment of Ritter's disease will be proved by its controlled use in large series of cases, especially of cases of the epidemic form.

CAPILLARY HEMANGIOMA WITH EXTENSIVE PURPURA

REPORT OF A CASE

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Benign vascular tumors may occur in any tissue in the body. The skin is the structure most commonly affected. From histopathologic studies, according to Stout,[1] hemangiomas of the skin may be divided into two groups: those of the capillary or telangiectatic type, which consist of numerous tubules lined by endothelium and surrounded by cellular intercapillary tissue of varying thickness, and those of the cavernous type, in which blood channels are irregular and more widely dilated. Lymphangiomas are mainly composed of capillaries containing lymph or of widened cystic lymph spaces. Not infrequently both lymph and blood vessel channels may be found in the same tumor, which is then described as a hemangiolymphangioma. The most characteristic feature of the angioma is its red or purple color, of varying intensity, which is due to the large blood content of the tumor.

Thrombopenic purpura associated with benign hemangioma is rare. In fact, we have not been able to find a record of a combination of these two conditions in the medical literature. We wish to report the following case of an extensive hemangioma of the skin associated with diffuse purpuric manifestations. The course and management of the condition, we believe, are of unusual interest.

REPORT OF CASE

History.—A. B., a boy born on Jan. 31, 1937, was admitted to the Babies Hospital on April 2, 1937, at 2 months of age. The chief complaint on admission was a lump in the left thigh, which had been present since the first week of life. The patient was the third of three children; the others were living and well. There was no known tuberculosis, syphilis or other familial disease. He was born at full term by spontaneous delivery, weighing 7 pounds 11 ounces

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1. Stout, A. P.: Unpublished data.

(3,487 Gm.). He had had no cyanosis, convulsions, hemorrhages or jaundice during the neonatal period. He was fed from birth on a whole milk dilution, with the addition of dextrimaltose. He received orange juice and cod liver oil for two weeks before admission. He held his head up at 6 weeks of age.

When he was 1 week old, there suddenly appeared a purple band of swelling about the upper third of the left thigh. This mass increased steadily in size, extending proximally and posteriorly to the left buttock, and in the week prior to admission it had reached the left inguinal region, then the scrotum and finally the right inguinal area. There was no tendency to distal extension down the thigh. The family physician advised hot compresses, and six weeks prior to admission he incised the mass in two places, obtaining only spurts of blood. The bleeding was easily controlled, and the incision healed promptly. There was no constitutional reaction, and the infant ate, slept and gained in weight normally.

Physical Examination.—The temperature was 99 F., the pulse rate 160 and the respiratory rate 60. The weight was 4,850 Gm. The patient was well developed and nourished, but appeared somewhat pale. His skin turgor was normal. In the upper third of the left thigh anteriorly, and extending around posteriorly to include all but the most medial portion of the left buttock, was an irregular lesion, which had a faintly reddish purple color and a sharply demarcated lower border above the left knee. This area continued across the inguinal crease to the scrotum, which was tense. The skin of the scrotum was thickened and stiff. The texture of the skin gradually became normal as the right thigh was approached and also up over the abdomen at a distance of 2.5 cm. above the symphysis, but there was no definite line of demarcation similar to that seen on the left thigh. The circumference of the left thigh at the area involved was larger than that of the right thigh at a corresponding level (fig. 1).

The red cell count on admission was 3,000,000 per cubic millimeter; the hemoglobin content was 10.2 Gm. (60 per cent Sahli) per hundred cubic centimeters; the leukocyte count was 10,050 per cubic millimeter, and the percentage of polymorphonuclear leukocytes was 27. The bleeding and coagulation times and the platelet count were not determined during the first ten days, since there was no indication that they would throw any light on the diagnosis.

It was the feeling of several observers that this was a most unusual lesion, and it seemed impossible to make a definite diagnosis, though a hemangioma was strongly considered as a possibility.

Roentgen Examination of Pelvis and Lower Extremities (April 3, 1937).—A large soft tissue mass was seen in the left thigh, extending down to the knee. It was made up of an irregular reticular pattern which extended beyond the borders of the shadows of the muscle bundles into the thickened tela subcutanea. No pathologic changes were present in the left femur. Below the left knee the soft tissue shadows appeared moderately swollen but showed no abnormal reticular pattern.

Course and Management of the Condition.—On April 7, 1937, five days after the infant's admission to the hospital, a biopsy specimen was taken from the mass on the thigh, which showed the tumor to be a capillary hemangioma, involving the corium and subcutaneous adipose tissue. The growth was made up of many lobules of fine capillaries, separated by cellular intercapillary tissue. In the latter, spindle-shaped cells supported by a delicate fibrillar stroma were numerous. In a few tumor cells mitotic figures were found.

On April 9, 1937, seven days after admission, numerous petechiae appeared over the lower part of the abdomen, and for the next four weeks the hemorrhagic area slowly increased until it assumed the proportions of a band encircling the body at a level of about 1.25 cm. below the midpoint of the clavicles. The mass on the left side slowly increased in size and extent, and there developed a brawny edema of the left leg, the ankle and the dorsum of the foot, with brownish pigmentation of the skin.

On April 12, 1937, the tenth day after admission, the red cell count was found to be 2,480,000 per cubic millimeter, the hemoglobin content 8.2 Gm. (48 per cent Sahli) per hundred cubic centimeters, the platelet count 48,000, the coagulation time six and one-half minutes and the bleeding time nine and one-half minutes. As thereafter the platelet count decreased and the bleeding and coagulation times increased, we felt that the petechiae which had appeared were

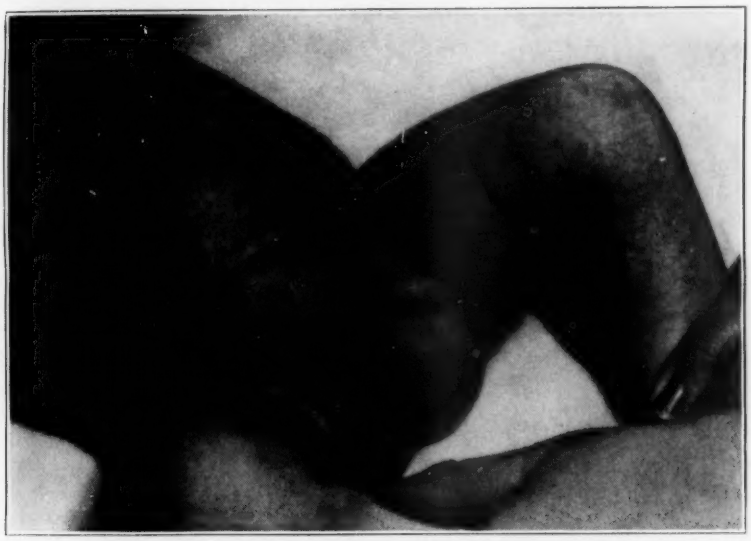

Fig. 1.—Lesion of the left thigh, showing enlargement, and discoloration of the skin. This discoloration is also seen in the skin of the lower part of the abdomen. (Compare this with fig. 3.) The patient was 2 months of age.

a manifestation of thrombopenic purpura, which was superimposed on the hemangioma.

In figure 2 is shown the general trend of the hemoglobin content, the red blood cell and platelet counts and the coagulation and bleeding times.

The results of laboratory and other examinations were as follows:

The culture of fluid aspirated from the area of fluctuation on the left thigh showed no growth.

The reaction to the Kahn test, both routine and presumptive, was negative.

The urine showed traces of albumin consistently. The specific gravity ranged from 1.012 to 1.020. Microscopic examination showed white cells ranging from an occasional one up to 4 and red cells varying from an occasional one up to 22 per high power field.

The temperature was elevated during the second, third, fourth, fifth, sixth, twelfth and thirteenth weeks of the infant's stay in the hospital, ranging from 99 to 104 F., but showed no consistent pattern. There were transient rises during the nonfebrile periods.

On April 20, 1937, Dr. Kesten, of the department of dermatology, felt that radium therapy should be used, since there was a possibility that the hemangioma was radiosensitive.

On April 21, 1937, the left thigh appeared about twice the size which it did on admission. From necrotic areas scattered over the thigh from groin to knee there oozed a foul-smelling serosanguineous discharge. The penis was swollen and bluish, and the scrotum seemed to be infiltrated with the tumor mass. The

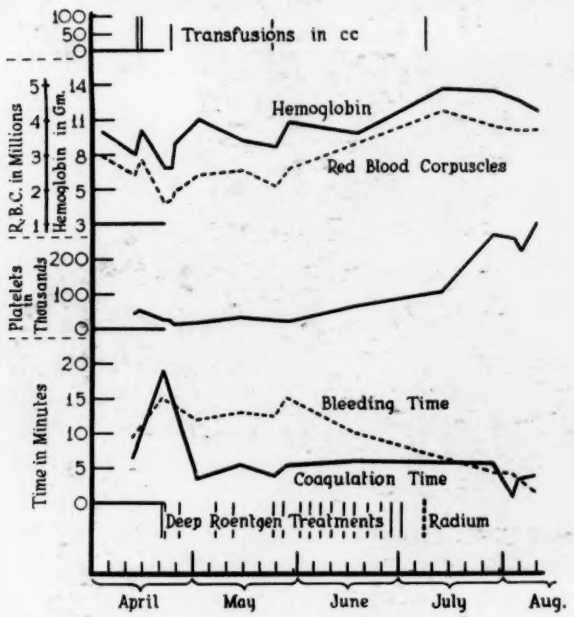

Fig. 2.—Curve showing red blood cell count, hemoglobin content, platelet count and bleeding and coagulation times and their relation to roentgen therapy, radium therapy and transfusions. (The bleeding time was estimated by the method of Duke. The coagulation time was determined by the fine capillary tube method.)

appearance of the lesion is best shown in figure 3. In spite of the apparently hopeless prognosis, it was finally decided to use roentgen ray therapy.

From April 21 to July 1, 1937, the patient received seventeen roentgen ray treatments. The region treated was the entire left lower extremity, including the boundaries of the lesion down to the ankle. In view of the low platelet count and because of the extensive nature of the hemangioma, small doses were administered and the entire region was divided into six small fields, varying from 6 by 8 to 10 by 10 cm. At the beginning of the course only one area was treated at daily intervals. From June 1 on, the treatments were separated by intervals of three or four days. Only on three occasions a field of 10 by 15 cm. was used

Fig. 3.—Lesion of the left leg, the scrotum and the abdomen, showing hemorrhagic appearance with a sharply demarcated line between the involved and the uninvolved area of skin of the thorax. The patient was 2¾ months of age. (Copied from a painting by June Thomas, M.D.)

UNIV. OF MICH.

on the ulcerated areas over the posterior-medial aspect of the left thigh. The technical factors were as follows: 130 kilovolts, 4 milliamperes, 27 cm. distance and a filter of 3 mm. of aluminum. The quantity varied from 75 to 100 roentgens (measured in air) per sitting per field. This plan was continued over a period of nine weeks, until each of the six fields had received approximately 300 roentgens measured in air. The lower part of the abdomen and the genitalia were not included in the fields of irradiation.

On May 12, 1937, less than six weeks after admission, the petechiae gradually faded, and only a faint brownish pigmentation remained over the lower part of the abdomen. However, the left thigh was still considerably larger than the right.

On July 1, 1937, the last roentgen ray treatment was given, and by this time the consistency of the upper part of the left leg had become softer. The true extent of the hemangioma could be outlined more satisfactorily after the subsidence of the purpuric discoloration. The purplish area was about 7 by 17 cm., of which the central portion, measuring about 4.8 cm. in diameter, contained yellow-green foul-smelling material.

On July 8, 1937, seven 4.4 cm. and six 3.2 cm. radium needles were inserted in and around the ulcerated hemangiomatous lesion on the posteromedial aspect of the thigh in such a manner as to produce uniform irradiation. The dose was estimated to be about 6 milligram hours per square centimeter. The total dose of interstitial radiation over an area of 7.7 by 17.8 cm. was 878.84 milligram hours.

From this time on, there was a gradual decrease in the size of the mass. (Figure 2 also shows the relation of irradiation, radium therapy and transfusions to the blood findings.)

On Aug. 6, 1937, roentgenograms showed that the tumor mass in the left thigh had decreased markedly in volume and had lost its reticulated structure, but the left thigh was still larger than the right.

On Aug. 10, 1937, the patient was discharged from the hospital, four weeks after the radium implantation, with the ulcerated area healed. The lesion on the posterior aspect of the left thigh occupied an area measuring 5.2 by 5.2 cm., which was still somewhat indurated and brawny. It faded into a band about 5 cm. wide of purplish pigmentation surrounding the rest of the thigh. The patient's lowest weight during his hospital stay was 4,400 Gm. (with a bandage). This occurred during a febrile period, and when the necrotic slough was present. He had gained only 1,310 Gm. during three and three-quarters months, as on discharge he weighed 6,160 Gm.

On Sept. 2, 1937, the condition of the lesion was as shown by figure 4, about two months after implantation of the radium needles and five months after the date of admission.

On Jan. 14, 1938, an orthopedic consultation was held (Dr. Howorth). The flexion deformity of the left hip was 30 degrees. Abduction and adduction were both limited 10 degrees. It was felt that the deformities would diminish. No treatment was advised.

On March 22, 1938, in the pediatric genito-urinary clinic the patient was circumcised.

On June 30, 1938, examination was made in the radiotherapy department. The patient, now 17 months of age, looked well, although slightly pale. He had twelve teeth. He walked well and showed no limp. The upper part of the anterior surface of the left thigh showed a faintly discolored area, measuring

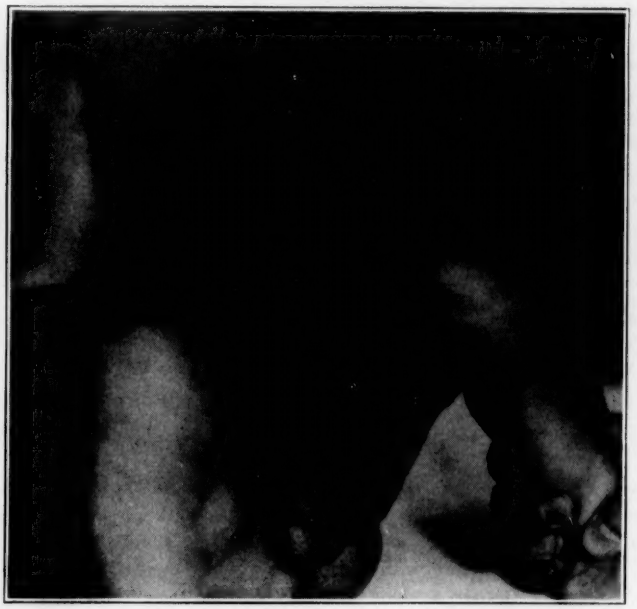

Fig. 4.—Discoloration and swelling of the left thigh are much improved after implantation of radium needles. The patient was 6 months of age when this photograph was taken.

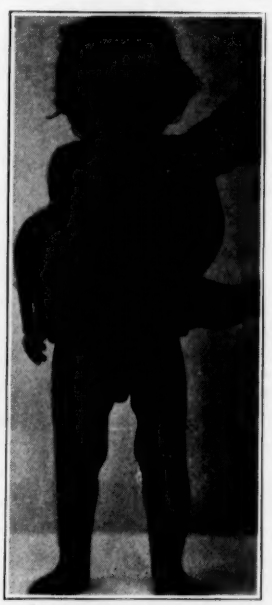

Fig. 5.—The infant at 21 months of age, showing scarring and atrophy of the left thigh.

14 by 9 cm. The central area was indurated, and the site of the previous ulceration was replaced by a scar. The periphery of the discolored area was smooth.

On Nov. 1, 1938, the patient aged 21 months, weighed 13,608 Gm. and was 83 cm. tall.

Laboratory data and the results of examination were as follows:

The red blood cell count was 4,590,000 per cubic millimeter, the hemoglobin content 13.6 Gm. (83 per cent Sahli) per hundred cubic centimeters, the platelet count 324,000, the coagulation time three minutes, and the bleeding time one minute.

The child seemed in excellent health and could jump, run and walk well. He had no limp. The circumference of the normal thigh (right) was 35 cm. just below Poupart's ligament, and that of the left at the same level was 30 cm. There was still a slight limitation of flexion of the left hip (fig. 5).

On June 2, 1939, roentgenograms of the pelvis and extremities were made, which showed no disproportion in the width and length of the bones on the two sides. The ossification centers were symmetric. No evidence of retardation of growth was demonstrated.

An orthopedic consultation was held (Dr. Howorth). The flexion of the left hip was 175 to 35 degrees, the abduction 25 degrees and the adduction 30 degrees. The internal rotation was 40 degrees and the external rotation 50 degrees. There was good muscle tone.

The scar in the left upper medial thigh was firm, inelastic, adherent and interfered slightly with the action and elasticity of adduction and with the function of the medial ham string muscles. The gait was normal.

COMMENT

An interesting feature of this case was the thrombopenic purpura, which appeared spontaneously before the vascular lesion on the leg was at its height. The fact that the platelet count reached a point as low as 16,000 and that the bleeding time was as long as fifteen minutes demonstrates the severity of the process.

The occurrence of purpura with malignant tumors is not infrequently seen. Recently a patient admitted to the Presbyterian Hospital with malignant hemangioma of the breast showed purpuric manifestations. Observers commented on the similarity of this patient to the one who is the subject of this paper.

Though the lesion of our patient was seemingly malignant, the results of biopsy did not substantiate this clinical impression, nor has the patient's course. We feel fairly certain, therefore, that this lesion was benign, although it is impossible to say whether the combined roentgen ray and radium treatment which this patient received was the deciding factor in combating a lesion which was or might have become malignant. It is to be noted that treatment was continued even though the platelet count was low.

SUMMARY

A case of extensive capillary hemangioma with associated thrombopenic purpura in an infant 2 months of age is reported. The extent and

rate of advance of the lesion and the presence of purpura suggested the possibility of a malignant vascular tumor. The benign nature of the mass was apparently proved by biopsy and by the patient's good health at 2½ years of age, but the exact role of radiotherapy in this case cannot be definitely stated.

The response of the lesion to external irradiation and radium therapy was very striking, despite a seemingly hopeless prognosis.

It seems reasonable to state that the judicial application of roentgen and radium therapy in small doses to a hemangioma with purpura has no deleterious effect on the low platelet count. Moreover, after the patient has been followed for over two years physical and roentgenographic examinations show that radiotherapy has in no way interfered with the normal course of osseous development.

The great importance of a biopsy of a lesion as extensive as this should be strongly emphasized.

LOCALIZED ABSENCE OF THE GANGLION CELLS OF THE MYENTERIC PLEXUS IN CONGENITAL MEGACOLON

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SAN FRANCISCO

The title of Hirschsprung's paper,[1] published in 1887, on the disease which bears his name reads, in translation, "Sluggishness of Stool in the Newborn Resulting from Dilatation and Hypertrophy of the Colon." It indicates what is now a well established fact, that there is a group of cases of so-called congenital megacolon in which, despite obvious manifestations of incomplete, localized intestinal obstruction occurring at various levels of the large bowel, no gross stricture or stenosis can be demonstrated. The absence of an organic, macroscopic cause for the obstruction is all the more striking in that almost identical manifestations are found in other cases in which a mechanical cause is evident, such as stricture, diaphragm formation of the rectal valves and inflammatory lesions causing chronic spasm.

No satisfactory explanation based on anatomic evidence has as yet been generally accepted, and recent discussions have dealt largely with a functional cause, particularly since Scott and Morton,[2] Wade and Royle,[3] Judd and Adson[4] and others have demonstrated that abolition of the sympathetic nervous impulses to the bowel by spinal anesthesia or removal of the sympathetic nerve supply frequently permits peristalsis and evacuation to be reestablished. No organic basis for this phenomenon has been offered. The concept of "sympathetic

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1. Hirschsprung: Stuhlträgheit Neugeborener in Folge von Dilatation und Hypertrophie des Colons, Jahrb. f. Kinderh. **27**:1, 1887.

2. Scott, W. J. M., and Morton, J. J.: Sympathetic Inhibition of the Large Intestine in Hirschsprung's Disease, J. Clin. Investigation **9**:247, 1930.

3. Wade, R. B., and Royle, N. D.: The Operative Treatment of Hirschsprung's Disease, M. J. Australia **1**:137, 1927.

4. Judd, E. S., and Adson, A. W.: Lumbar Sympathetic Ganglionectomy and Ramisectomy for Congenital Idiopathic Dilatation of the Colon, in Collected Papers of the Mayo Clinic and the Mayo Foundation, Philadelphia, W. B. Saunders Company, 1928, vol. 20, p. 288.

overactivity" or some other imbalance of intestinal innervation, while probably correct, leaves the underlying cause of the disturbance entirely unexplained.

The possibility that the disorder may be due to a localized nerve lesion has been frequently mentioned and discussed by reviewers, but almost as often discarded on the grounds that such lesions have not been found by some investigators when they were looked for. Scrutiny of the available evidence has, however, convinced us that the negative reports available are not crucial, because in none of them is it stated that the portion of the intestinal wall at or immediately distal to the site of obstruction was examined to determine the state of the nerve elements there. On the other hand, we do not believe that the positive reports should be disregarded.

Gee [5] in 1884, reported the occurrence of idiopathic dilatation of the large intestine in a child. This report is often cited as disproving the theory of a nerve lesion. Gee, however, merely stated that the "diameter of the widest part of the sigmoid was about 4 inches; its muscular coat and nerves were greatly hypertrophied."

In 1901 Tittel [6] described the occurrence of dilatation and hypertrophy, without demonstrable stenosis, of the large bowel, including the upper half of the rectum, in an infant dying at the age of 15 months. He noted that the ganglion cells of the myenteric plexus at various levels of the large intestine were scanty and showed some degenerative changes which he thought were not due to faulty preservation, because a sympathetic ganglion lying outside the rectum was well preserved. Tittel noted that the condition of the ganglion cells was normal only in the ileum. He concluded that the abnormal state of the myenteric plexus might have influenced unfavorably the normal course of peristalsis.

Finney [7] in 1908 resected most of the colon of a 9 year old boy. He found the ganglion cells of Auerbach's plexus to be normal in several sections and added, "If anything the cells were larger than normal." It is clear that the sections were taken from the hypertrophied portion of the colon and not at or below the point of obstruction. Schmidt,[8] in 1908 found the ganglion cells to be normal in number in 4 cases, but he, too, failed to state from which part of the bowel the sections were taken.

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5. Gee, A.: Idiopathic Dilatation of the Large Intestine, St. Barth. Hosp. Rep. **20**:19, 1884.

6. Tittel, K.: Ueber eine angeborene Missbildung des Dickdarmes, Wien. klin. Wchnschr. **14**:903, 1901.

7. Finney, J. M. T.: Congenital Idiopathic Dilatation of the Colon, Surg., Gynec. & Obst. **6**:624, 1908.

8. Schmidt, J. E.: Ueber Hirschsprung'sche Krankheit, insbesondere ihre chirurgische Behandlung, Beitr. z. klin. Chir. **61**:682, 1908-1909.

Retzlaff [9] in 1920 examined sections from a greatly dilated sigmoid colon removed surgically and found the ganglion cells to be normal. Here, as in Finney's case, it is obvious that the sections were taken well above the point of obstruction.

In 1920 Dalla Valle [10] reported a case of megacolon in which the patient died at the age of 10½ months; in 1924 [11] he reported the occurrence of the same condition in the child's brother. In both cases many sections of various portions of the large intestine were carefully examined, with special reference to the nerve cells of the myenteric plexus. This was the first time that a really comprehensive study had been made. The changes observed, which closely resemble those in our case, are of great interest. In the first case the ascending, transverse and descending portions of the colon were greatly enlarged, but the sigmoid flexure was of normal caliber. In the ascending colon the cells of Auerbach's plexus were few and small; in the transverse and the descending colon they were normal in appearance, while in the sigmoid colon they were absent. In the second case the extent of enlargement was almost exactly the same; the transition from the descending colon to the sigmoid colon was sharply marked, and within a linear distance of 3 cm. the intestinal caliber returned to normal. The cells of Auerbach's plexus were normal in numbers in the appendix, cecum and ascending, transverse and descending colon, but in over a hundred sections from the sigmoid colon none could be found.

Brentano [12] in 1904, studying the intestines of a 14 year old girl, found that the nerve elements in the large intestine were weakly developed but failed to state from what part the sections were taken.

In 1928 Cameron [13] reported dilatation extending from the cecum to the pelvirectal sphincter in a 10 year old boy. The cells of the myenteric plexus in the dilated portions of the bowel appeared normal, but in the region of the pelvirectal sphincter they were absent, having been entirely replaced by inflammatory cells. Cameron concluded that the destruction of the nerve cells had acted as an obstacle to peristalsis.

In 1938 Robertson and Kernohan [14] stated that in a case of megacolon sections from the transverse colon and the sigmoid colon showed

9. Retzlaff, K.: Zur Hirschsprung'sche Krankheit, Berl. klin. Wchnschr. **57**:319, 1920.

10. Dalla Valle, A.: Ricerche istologiche su di un caso di megacolon congenito, Pediatria **28**:740, 1920.

11. Dalla Valle, A.: Contributo alla conoscenza della forma famigliare del megacolon congenito, Pediatria **32**:569, 1924.

12. Brentano: Ueber einem Fall von Hirschsprung Krankheit, Verhandl. d. deutsch. Gesellsch. f. Chir. **33**:265, 1904.

13. Cameron, J. A. M.: On the Aetiology of Hirschsprung's Disease, Arch. Dis. Childhood **3**:210, 1928.

14. Robertson, H. E., and Kernohan, J. W.: The Myenteric Plexus in Congenital Megacolon, Proc. Staff Meet., Mayo Clin. **13**:123, 1938.

degenerative changes in the cells and fibers of Auerbach's plexus and that in some sections the cells were absent. They remarked that similar changes were found in several other cases. Unfortunately, complete details are lacking in their report.

Since the myenteric plexus extends throughout the alimentary tract from the esophagus to the rectum and since the peristaltic mechanism is likewise similar throughout, it seems pertinent to call attention to lesions that have been found in cases of esophagectasia and cardiospasm and to the similarity between such cases and those of megacolon. Hurst [15] in 1924 expressed the opinion, without reporting any direct observations, that achalasia of the esophagus is usually caused by progressive organic disease involving Auerbach's plexus. He has also stated [16] the opinion, based on relief obtained from rectal dilatation with specially designed bougies, that megacolon is usually due to achalasia of the rectum. He has not, however, presented any anatomic or histologic studies in support of this contention. In 1926 Rake [17] noted hypertrophy without dilatation in a man 67 years of age who died of cancer of the tongue but had had no difficulty in swallowing. Microscopic examination showed the esophagus to be normal above the level of hypertrophy, but inflammatory changes were present in the hypertrophied portion, being most marked in the ganglions. Many of the nerve cells had disappeared; others were disintegrating, and there was an unusual cellularity of the nerve sheaths.

Cameron [18] in 1927 reported esophagectasia and cardiospasm in a child who died at the age of 6 years. Microscopic examination showed an acute inflammatory process involving the cells of the myenteric plexus in the esophagus, while those in the pyloric and the pelvirectal area were normal. In 1932 Amorim and Netto [19] reported a case of megaesophagus and dilatation of the colon and rectum in which the conditions had apparently developed during convalescence from typhoid fever. They found generalized atrophy of the myenteric plexuses throughout the alimentary tract. The ganglion cells were diminished in numbers and in places were completely lacking. About the nerve fibers of the plexus in the lower portion of the esophagus and the last part of the rectum

15. Hurst, A. F., cited by Rake.[17]

16. Hurst, A. F.: Anal Achalasia and Megacolon, Guy's Hosp. Rep. **84**:317, 1934.

17. Rake, G. W.: A Case of Annular Muscular Hypertrophy of the Oesophagus (Achalasia of the Cardia Without Oesophageal Dilatation), Guy's Hosp. Rep. **6**:145, 1926.

18. Cameron, J. A. M.: Oesophagiectasia in a Child, Arch. Dis. Childhood **11**:358, 1927.

19. Amorim, M., and Netto, A. C.: Histopathologia e pathogenese do megasophago e megarecto (consideraçoes em torno de um caso de "Mal de engasgo"), Ann. Fac. de med. de São Paulo **8**:101, 1932.

there was round cell infiltration. In 1934 Etzel [20] reported 8 cases of megaesophagus and noted degenerative changes in Auerbach's plexus in all. In 4 of these there was coexistent megacolon. In 1937 he reported [21] 14 cases of megaesophagus, in 8 of which megacolon was also present. In all of these, degenerative changes were found in Auerbach's plexus.

Finally, we cite the case reported in 1935 by Perrot and Davon [22] in which an infant died on the fifteenth day of life and about six hours after operation for intestinal obstruction, having had obstipation, abdominal distention, abdominal pain and fecal vomiting. The stomach, the pylorus and the duodenum were normal. The small intestine was thickened and distended down to a point 10 cm. above the ileocecal valve, where it became constricted. The myenteric plexus was well developed and normal in appearance throughout the hypertrophied part of the bowel, but nerve cells became rare at the point of beginning constriction and down to the splenic flexure, after which they became more numerous and regularly spaced. The authors expressed the belief that hypoplasia of Auerbach's plexus had caused a functional obstruction.

REPORT OF A CASE

M. R., a white boy born on April 1, 1937, was first seen by us on April 12, 1938. The presenting complaints were constipation and abdominal distention beginning soon after birth.

The family history was unimportant. The birth had been normal, and the birth weight was a little over 7 pounds (3,175 Gm.).

The infant refused to take fluid as early as the first day. On the seventh day he was operated on for intestinal obstruction, but none was found. After recovery the stools were infrequent, abdominal distention was present and at 1 month there were two attacks of fecal vomiting. Roentgenograms taken after an enema of barium sulfate at 5 weeks showed no obstruction, and a proctoscopic examination at about the same age showed nothing abnormal. At the time the infant was 3 months of age the abdomen was protuberant, and the stools were still infrequent.

In October 1937 the results of another barium enema were interpreted as showing a "mechanical obstruction." In December a "huge" fecal impaction had to be removed. Another barium enema on December 6 showed progressive dilatation of the large bowel above the sigmoid colon.

During this period and up to the time we first saw the patient, the mother had given him frequent enemas combined with abdominal massage. Solid material

20. Etzel, E.: Neuropatologia do megaesôfago megacolo, Ann. Fac. de med. de São Paulo **10**:383, 1934.

21. Etzel, E.: Megaoesophagus and Its Neuropathology: A Clinical and Anatomo-Pathological Research, Guy's Hosp. Rep. **17**:158, 1937.

22. Perrot, A., and Davon, L.: Obstruction intestinale de cause rare, chez un nourrison, Ann. d'anat. path. **12**:157, 1935.

was always difficult to evacuate; fluid sometimes returned in fair amounts, but a good deal of this also was retained. The child had a poor appetite and failed to gain properly in weight and strength. The abdomen became progressively more distended. Vomiting was frequent, especially after enemas. The diet offered was adequate and had been supplemented with ascorbic acid, thiamin (betaxin), purified vitamin D in propylene glycol (drisdol) and an iron preparation. Black particles were present in the stools and had persisted for two weeks after the iron had been stopped.

Physical Examination.—The boy was thin, weighing 8,650 Gm. There was some flattening of the head posteriorly and on the right side. There were four upper and two lower incisors. There were no signs of rickets or scurvy. No other important abnormalities except those in the abdomen were noted.

The abdomen was enormously enlarged, and active peristaltic movements, apparently of the small intestine, could be seen frequently in its thin walls, often accompanied by peristaltic gurgles. The liver and the spleen could not be felt.

The urine was normal. The blood count showed 4,770,000 red cells, 14.58 Gm. of hemoglobin per hundred cubic centimeters (85 per cent Sahli) and 10,300 white cells, with 35 per cent polymorphonuclears (10 per cent banded), 60 per cent lymphocytes and 5 per cent mononuclears. The stool gave a 1 plus reaction to an occult blood test and was otherwise normal.

A barium enema was given on April 15, 1938. Dr. R. R. Newell's report reads:

"The abdomen is very large, and preliminary films show that this is due to an enormous distention of the large intestine with gas.

"The barium enema runs readily back through the colon to the cecum. The sigmoid flexure is long and of normal diameter. The colon widens very suddenly to a marked dilatation. This sudden change occurs in the left iliac fossa. I cannot make out any organic obstruction. In fact, barium runs back through this area quite readily. Referring to the old films, we note that the ascending, transverse and descending colon show progressing dilatation.

"Conclusion: The marked dilatation is limited to the colon above the sigmoid flexure. There is no roentgen evidence of organic obstruction."

There was no fever during the child's four day stay in the hospital. It was found that rectal instillations of liquid petrolatum helped the evacuation of softened stools. Enemas of water were largely retained, and attempts at siphonage with a rectal tube were only partly successful. The child was placed on a nearly nonresidual diet and sent home with instructions for the use of the periodic rectal instillations of oil, abdominal massage and a rectal tube.

On this regimen the child gained 5 pounds (2,268 Gm.) during the next month but required constant attention and much care to avoid serious distention and impaction. His condition became sufficiently discouraging for him to be brought back to the hospital on May 30. At this time syntropan, as recommended by Klingman,[23] was given in doses of 5 to 20 mg. daily. No favorable results were obtained, and the drug was discontinued after five days. Three days later 0.2 mg. of prostigmine was given hypodermically. Fifteen minutes later powerful contractions, apparently of both the large and the small bowel, were seen, and loud borborygmi were heard; however, during the next twenty-five minutes no flatus or fecal material was expelled. The contractions caused

23. Klingman, W. O.: Treatment of Neurogenic Megacolon with Selective Drugs, J. Pediat. **13**: 805, 1938.

pain. A rectal tube was inserted, and about 10 cc. of fluid and a good deal of gas escaped. The waves, which showed no consistent direction, persisted in gradually diminishing strength for about six hours.

Two days later (on June 8), 10 mg. of procaine hydrochloride was given intrathecally, an amount which proved not enough to produce anesthesia or paralysis of the legs. However, peristaltic waves occurred which were similar to but less vigorous than those produced by the injection of prostigmine and were likewise ineffective in producing an evacuation of gas or stool.

A second attempt to produce spinal anesthesia was made the next day, 15 mg. of procaine hydrochloride being used, but it was unsuccessful and resulted in only slight peristalsis.

On July 4, the boy was returned to the hospital for lumbar sympathectomy. His condition at this time was unchanged. His weight was 9,500 Gm. (21 pounds), and his height was 78.5 cm. (31 inches). It was felt that the operation was justified on the grounds of the partial success obtained with spinal anesthesia in promoting peristalsis and that it offered the best chance of relieving a condition which was plainly serious and had failed to be ameliorated by medical measures. Left lumbar sympathectomy was done on July 5 by Dr. L. R. Chandler and Dr. F. L. Reichert by the Flotow (extraperitoneal) operation. The sympathetic chain was exposed from the upper branches of the first lumbar nerve downward past the fourth lumbar ganglion, and the chain and rami were removed.

There was considerable loss of weight, but the postoperative course was on the whole uneventful. No definite immediate benefit in evacuation occurred. The child was sent home on July 10.

His progress during the summer was decidedly encouraging. The mother wrote on September 16 that he was having a "daily elimination" of one to four stools without any enemas or catharsis, that he was much stronger and more active and that his appetite was better. He had not, however, gained any weight. By October 16 his condition was again unsatisfactory. Distention and infrequent stools had recurred and could not be relieved by enemas or cathartics (cascara). His condition became progressively worse, and he was readmitted to the hospital on December 3.

An enema of a 25 per cent solution of thorium dioxide showed that the right side of the colon was larger than ever and that the entire colon down to the sigmoid flexure was immense. On entry to the hospital the patient's weight was 11,793 Gm. (26 pounds), but after colonic lavage and removal of a large amount of feces it was reduced to 10,432 Gm. (23 pounds) five days later. Acetyl-betamethylcholine chloride (mecholyl) was administered. It produced powerful contractions like those obtained previously with prostigmine and with procaine hydrochloride, which were likewise ineffective in causing evacuation. The abdomen was more distended than on previous entries, and the great intra-abdominal pressure interfered with the proper action of the diaphragm, making the respirations shallow, rapid and labored. Another attempt to produce spinal anesthesia, this time with 30 mg. of procaine hydrochloride, caused paralysis and anesthesia of the extremities and resulted in some peristaltic waves, apparently mainly in the ascending colon.

The child's condition was now obviously desperate. His appetite had failed, and there was some vomiting and dehydration, for which parenteral fluids were given. On December 20 his temperature (rectal) rose to 38.4 C. (101.1 F.) without obvious cause other than dehydration. A roentgenogram of the chest at this time showed no pathologic conditions. It was decided as a last resort to remove the first, second and third ganglions of the right sympathetic chain, and this was done

on December 21 by Dr. Chandler and Dr. Reichert, who used the extraperitoneal approach. Four hours after operation the child showed pallor, prostration and rapid pulse. Despite various supportive measures his condition became rapidly worse, and he died about twenty-seven hours postoperatively, on December 22.

Summary of Case.—The essential features of the case may be summarized as follows: Constipation and progressive abdominal distention beginning soon after birth, leading to death at the age of 20 months, 3 weeks; roentgenographic evidence of progressive dilatation of the entire large intestine above the sigmoid flexure without obstructive stenosis; absence of effect from a parasympathetic depressant (syntropan); production of powerful intestinal contractions without propulsion of contents by parasympathetic augmentor drugs (prostigmine and mecholyl) and by sympathetic depression (spinal anesthesia); and failure of left and of right lumbar sympathectomy to relieve condition.

Necropsy (Dr. William Dock).—Macroscopic Examination: The body was that of a thin and poorly developed infant with an enormously distended abdomen and a widely flaring thorax. The infant looked less than 18 months old but had six incisor teeth. The hair on the scalp was moderately abundant, and the pupils, nares, ears and mouth were not remarkable. The neck and limbs were thin and with the huge belly gave a spidery appearance. The genitalia were normal for a male infant.

There was a fine white scar in the left side of the abdomen and a fresh surgical incision, silk-closed, on the right side halfway from the navel to the iliac crest. There was scarcely any subcutaneous fat in the midline incision. The omentum covered most of the bowel and was adherent to a small area on the left lower anterior part of the wall and to the mesentery of the ileum near the cecum. There were no constricting bands or intra-abdominal hernias. The lower 1.5 meters of the ileum was distended with gas and was over 3.5 cm. in diameter. This distention ended abruptly, but no constricting band or kink was found at the point of transition into empty bowel. The duodenum and stomach were also empty. The cecum, distended with gas and semisolid feces, was over 8 cm. wide. The appendix was free and not remarkable. The ascending, transverse and descending colon were likewise distended with thick, putty-like feces and varied from 4 to 9 cm. wide. The walls seemed abnormally thick. The distention ended abruptly at the beginning of the sigmoid colon, which was empty and had a wall normally thick for that state. At the rather sharp point of transition there was no scar, band or other visible cause; pressure on the descending colon easily forced the fecal material downward, distending the sigmoid colon to twice its original diameter.

The edge of the liver was not visible until the transverse colon was lifted up, when it was found to be pressed far up and back, with its normal lower surface facing anteriorly. The diaphragm was pushed up to the level of the third rib on each side. There was a little fluid in the left pleural cavity and only a few centimeters of fluid in the pericardium.

The left sympathetic chain ended in a small mass of scar tissue in the lower edge of the diaphragmatic attachment along the spine. The right chain ended at the semilunar ganglion, and the four lumbar ganglions were absent. There was scarcely any fresh blood in the incision leading to this area. A small peritoneal tear was closed with silk.

The heart weighed 40 Gm. There was a trace of subepicardial fat. The endocardium throughout was normal, as were the valve leaflets. The myocardium of the left ventricle was 4 to 5 mm. thick, uniform red and of moderately firm consistency. That of the right ventricle was 2 mm. thick; otherwise it was similar

to the left. The foramen ovale was closed. The pulmonary artery contained a postmortem clot. No remnant of the ductus arteriosus was found. The sinuses of Valsalva, the base of the aorta and the coronary arteries were not remarkable. The combined weight of the two lungs was 120 Gm.; they were crepitant and free of adhesions and consolidations, and the cut section revealed a moderately dry, grayish pink surface. The bronchi and branches of the pulmonary artery were not remarkable.

The liver weighed 340 Gm. The capsule was smooth and a reddish purple. On cut section the surface was of normal consistency and a pale tan. The markings were indistinct. The branches of the portal venous system and bile ducts were patent. The gallbladder contained 3 to 5 cc. of rather thin, dark bile. The mucosa had the usual velvety character.

The duodenum contained a trace of bile-stained chyme. The stomach was empty. The mucosa of both was normal. The spleen weighed 18 Gm. The capsule was finely wrinkled and slate gray. The cut surface was of normal consistency and showed prominent malpighian markings. The pancreas was of normal size, and the cut section showed a tan, lobulated surface. The adrenal glands were of normal size, and the cut section showed scant, pale lipoid.

The combined weight of the two kidneys was 50 Gm. Fetal lobulations were prominent. The capsules stripped with ease, revealing a smooth surface. On cut section the markings were sharp, and the cortex was 4 to 5 mm. thick. The pelves and ureters were glistening, white and not dilated. The urinary bladder contained about 25 cc. of slightly cloudy urine. The mucosa and wall were not remarkable.

The small bowel was partially filled with gas and semiliquid, brown feces. The mucosa was normal. The large bowel, including the cecum and the colon, was 145 cm. long. The proximal distended portion was 110 cm. in length, whereas the normal appearing sigmoid colon was 35 cm. long. The greater circumference of the large bowel was in the transverse colon, where it measured 24.5 cm. The contents of the large bowel weighed 1,460 Gm. and consisted of putty-like, pale yellow feces. The lower part of the sigmoid colon was free of fecal material. At the point of transition between the large and the normal appearing bowel there was no visible constricting abnormality. The mucosa and wall here both appeared normal. The mucosa of the distended bowel was moderately injected and showed ill defined, pale brown circular areas scattered throughout. These were 1 to 2 mm. in diameter. The mesentery contained a large number of moderately firm lymph nodes ranging up to 2 cm. in diameter. On cut section these were uniform gray.

The arch of the aorta was of good elasticity and free of plaques.

Histologic Examination: The heart was normal.

A section from the lower lobe of the right lung showed alveoli with thick, hyperemic septums. Many of the alveoli were filled with fibrin, enmeshed in which were unrecognizable disintegrating cells, a few lymphocytes, phagocytes and an occasional polymorphonuclear leukocyte. Some of the alveoli of the section were partially collapsed. The bronchi were filled with desquamated epithelial cells, red cells, a few lymphocytes and leukocytes. All other sections of lung showed alveoli with thickened, hyperemic and edematous septums. A few of the alveoli were partially filled with edematous fluid. The bronchioles were subtotally filled with fibrin and disintegrating leukocytes, erythrocytes and lymphocytes. The bronchioles were surrounded by a few macrophages and lymphocytes. The pleura was free of exudate.

The liver cells of the central portion of the lobule stained well and showed distinct nuclei. Those about the periphery contained large, clear vacuoles, with displacement of the nucleus to the periphery of the cell. A few of the cells contained multiple small vacuoles. All the vacuoles were shown by fat stain to be filled with fat.

In the spleen malpighian bodies were numerous but not sharply outlined. The pulp was moderately distended with red blood cells. A few lymphocytes and an occasional leukocyte were seen in the sinuses. The capsule was of normal thickness. The pancreas was normal.

The glomeruli of the kidneys were normal. The tubular epithelium was swollen and the cytoplasm slightly granular. A few of the tubules contained a granular, eosinophilic substance.

The mesenteric lymph nodes showed large follicles but no germinal centers. The peripheral and the medullary sinuses were loosely packed with small lymphocytes.

Sections, along a taenia coli, of the terminal portion of the dilated colon and the grossly normal portion of the sigmoid colon showed a few scattered ganglion cells of Auerbach's myenteric plexus lying between the circular and the longitudinal muscle only in the undilated sigmoid colon but none in the 7 cm. above this region. A section taken from the dilated transverse colon showed many ganglion cells. There was marked hypertrophy of the external muscle layers, the circular ranging up to 3 mm. in thickness and the longitudinal to slightly more than 1 mm. The mucosa was missing at the surface but was present in the crypts. The lamina propria contained many phagocytes laden with a granular brown material and was slightly infiltrated with lymphocytes and macrophages. The submucosa showed moderate fibrosis.

The semilunar ganglion was normal.

The follicles of the retroperitoneal lymph nodes were clear. None showed germinal centers. The sinuses stood out sharply. Those at the periphery contained large numbers of lymphocytes. The medullary cords contained a few scattered lymphocytes.

Diagnosis.—On the basis of clinical evidence a diagnosis of megacolon was made. On the basis of anatomic evidence a diagnosis was made of congenital megacolon, chronic lymphadenitis of the mesenteric lymph nodes, acute bronchitis and mild bronchial pneumonia.

Comment.—This is a case of congenital megacolon in which the point of transition to normal bowel was in the upper part of the sigmoid colon, not in the rectum, which usually is the site of the functional narrowing. At the point where the dilated bowel passed into that of normal caliber there were, for a distance of from 5 to 7 cm., no ganglion cells, but unusually abundant nerve fibrils were present in the Auerbach tissue. Elsewhere the ganglion cells were normal, both above and below the point where normal sigmoid colon and dilated bowel met. The colon was thick and large enough for a man; the thoracic content was displaced upward.

OBSERVATIONS

The cases cited from the literature and the case which we have reported strongly suggest that in at least some cases of megacolon and of related disorders, such as cardiospasm and megaesophagus, the primary disturbance is a localized interference with the passage of normal peristaltic waves across a given segment of the alimentary tract due to

defective innervation. This interference might consist of an inability of the musculature either to relax (achalasia) or to contract, either of which disturbances would prevent the sequence of alternate relaxation and contraction composing the peristaltic wave, and thus to render effective propulsion of intestinal contents across the involved segment. For all practical purposes the result of such a disturbance is an obstruction, even though no actual narrowing of the lumen can be demonstrated by roentgenogram, proctoscopy or postmortem examination. The "functional" obstruction, to be sure, is rarely complete and for a time may hardly be troublesome. Indeed, many patients live for considerable periods of time, even into adult life. As a rule, however, the obstructive difficulty gradually increases, dilatation and hypertrophy proximal to the lesion increase in degree and extent and various secondary disturbances of nutrition and general health supervene.

The nature of the disturbance of control of intestinal motility by the nervous system which should be expected from a localized absence of the cells of the myenteric plexus is difficult to discover from a review of such physiologic and pharmacologic experiments as we have found in the literature. Indeed, we have found no experimental work which is accurately comparable to the condition under consideration. It should be recalled that the cells of the myenteric plexus are the lower motor neurons of the parasympathetic system. Section of the extrinsic parasympathetic nerves, that is, of the upper motor neuron, would of course merely remove the central control of the Auerbach cells without paralyzing or destroying them. Paralyzing parasympathetic drugs, such as atropine and syntropan, cause general depression of peristalsis, and for practical purposes their effect is equivalent to reduction or abolition of the action of the Auerbach cells throughout most of the gastrointestinal tract. To determine the effect of localized absence of these cells over long periods, however, further experiments will be required.

Without attempting to theorize too much at the present time, it would seem fair to assume that the conditions set up by localized absence of the myenteric cells would involve (1) the local absence of parasympathetic action, presumably a local depression of peristaltic propulsion, or at least interference with the passage across the affected area of peristaltic waves, and (2) the locally unopposed action of sympathetic nervous impulses, assuming that sympathetic and parasympathetic functions are mutually antagonistic at the given point. This may be the explanation of the apparent "sympathetic overactivity" postulated by Judd and Adson.

Section of the sympathetic nerves obviously would leave the musculature in the affected region without nerve supply and the rest of the bowel supplied by the cut sympathetic nerves with parasympathetic innervation alone. It is conceivable that such an operation might relieve

local achalasia due to lack of the myenteric plexus, although it failed to do so in our case. On the other hand, it is possible that cases like ours form but one subgroup of cases of megacolon and that the underlying mechanism in others is quite different.

SUMMARY AND CONCLUSIONS

A case is described of megacolon in which the sigmoid flexure was of normal caliber and the entire colon above that segment was enormously dilated and hypertrophied. The production of spinal anesthesia, and the administration of mecholyl and prostigmine caused contraction of the bowel without propulsion of its contents. Sympathectomy did not influence the condition favorably. Syntropan had no definite effect.

The cells of Auerbach's plexus were normal in number and appearance throughout the hypertrophied and dilated portion of the bowel but were greatly diminished or absent in the undilated sigmoid colon.

This case and some others similarly studied indicate that a subgroup of cases of Hirschsprung's disease exists in which localized absence of the peripheral neurons of the parasympathetic system causes a functional partial obstruction in the same region, with secondary dilatation and hypertrophy in the bowel cephalad to it. It is uncertain what proportion of cases of Hirschsprung's disease belongs in this category.

The condition described appears to be closely related to that existing in cardiospasm with megaesophagus.

Progress in Pediatrics

GONORRHEAL VAGINITIS IN CHILDREN

A REVIEW OF THE LITERATURE

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A previous review (Benson and Steer, 1937) of the literature on gonorrheal vaginitis in children covered the more important contributions up to 1936. Reviews of the literature have also been published by Thomas and by Reichert and his associates. Since the time of those reviews there has been widespread interest in gonorrheal vaginitis, and new methods of diagnosis and treatment have resulted. Recent publications on the normal anatomy of the genital tract and the pathologic anatomy of gonorrheal vaginitis have produced valuable information. Because of these new contributions it has seemed worth while to bring the review up to date.

INCIDENCE

The previous survey indicated that gonorrheal vaginitis in children was of frequent occurrence. Since the time of its publication the following authors have supported that contention: Rice, 1,200 cases in hospitals, clinics and child-caring institutions of New York in 1936; Rosenthal and Weinstein, 343 reported cases in New York in 1938; Karnaky, 200 cases in Houston, Texas, in 1936; Hoffman and his co-workers, 150 cases a year in Cook County Hospital, Chicago. However, within the last year some evidence has been offered which indicates that this reported incidence probably includes cases of nonspecific vaginitis. It is suggested that when more strict criteria of diagnosis are used, such as will be discussed later, the incidence is found to be smaller. Thus the report of the London County Council indicates that only 148 instances of true gonorrheal vaginitis in children were discovered in London in 1935. Nabarro studied a series of 1,218 cases of vaginitis and of these found only 249 in which the infection was

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gonococcic and 21 in which the cause was doubtful. At the Metropolitan Hospital in 1938 there were 250 patients admitted with a diagnosis of gonorrheal vaginitis. Of these only 67 proved to have a gonococcic infection. It is apparent that considerable study will be necessary before satisfactory statistics will be available.

SOURCE OF INFECTION

We do not find in the recent literature new approaches to the study of the source of infection in gonorrheal vaginitis. The familiar sources are constantly accused, some additional data being presented. The importance of infection in the home has been further emphasized by Reichert and his associates, by Burpee, Robinow and Leslie and by Benson. It seems that such "gonorrheal nests" are probably the most frequent source of infection, although no one has clearly demonstrated just how the gonococcus reaches the child from the infected adult.

AGE LIMITS

It is known that gonorrheal vaginitis can occur at any age from birth until puberty. However, in contrast to gonorrheal ophthalmia, gonorrheal vaginitis is comparatively infrequent in the neonatal period, even when the mother in confinement has shown evidence of gonorrhea. To the few reported cases of gonorrheal vaginitis at birth 2 more have been added by Lewis and Adler (1936), although in these cases the vaginal discharge did not appear until two or three weeks after birth. Saxl reported the occurrence of gonorrheal vaginitis in an infant 4 days old.

COLLECTION OF MATERIAL FOR BACTERIOLOGIC DIAGNOSIS

The wet method of collecting material for bacteriologic diagnosis (Benson and Steer, 1939) has been found to be superior to the use of cotton applicators in obtaining material for smears and culture. This consists of inserting an ordinary glass catheter into sterile physiologic solution of sodium chloride. On removal it will be found that an amount of solution from ½ to ¾ inch (1.3 to 1.9 cm.) high has remained in the catheter, which is then introduced as far as possible into the vagina. The catheter on removal will be found to contain suspended in the solution varying amounts of vaginal discharge. The advantages of this wet method are: (1) that the instrument is easily inserted into the vagina; (2) that it does not cause pain or trauma; (3) that only one application is necessary to obtain material for smear and culture, and (4) that the true characteristics of the discharge can be easily recognized by the suspension in the saline solution.

ANATOMY

Since the last report there have been several contributions to the knowledge of the anatomy of the genital tract. Herrnberger found that a low vaginal mucosa and a predominance of white blood cells were characteristic of the vagina in childhood. He also found an inverse relation between the white blood cells and the layers of the epithelium. During childhood little desquamation occurs; the vaginal secretion at this time will contain some epithelial cells which stain poorly, as well as free epithelial nuclei and products of nuclear degeneration. However, as the child grows older and approaches puberty the vaginal secretion will increase and will contain large, well staining epithelial cells which are derived mainly from the stratum spinosum and from the layer of karyopyknotic cells of the vagina.

Benson, Steer and Speer performed an autopsy on a 3½ year old child, supporting their observations by vaginoscopic examination. Besides the known facts that the cervix and vagina are relatively long as compared with the rest of the genital tract, they emphasized the importance of the vaginal rugae, the shape of the cervix and the presence of endocervical glands. The large number of vaginal rugae were found to extend over the vaginal surface of the flattened cervix.

Dobszay stated that the external os of the cervix is closed during childhood until the onset of puberty and that it is owing to this fact that inflammatory processes in the vagina seldom extend into the cavity of the uterus or above. Some authors believe the closure is due to cellular adhesions in the cervical canal, while others believe it is due to a mucous comedo which fills the cervical canal. Dobszay expressed the belief that this obstruction is due to an elastic contraction of the cervix which is not present in newborn infants. In the latter the cervix remains patent during the first three weeks of life, a fact which Dobszay attributed to the action of estrogen still circulating in the infant.

PATHOLOGY

Santalow and Nowotelnowa performed autopsies on 9 children who had gonorrheal vaginitis; 3 had subacute infections which lasted from three to six months, and 6 had chronic gonorrhea with a duration of from six to eighteen months. The children's ages were from 18 months to 3 years. The authors found that the areas most affected were the posterior portion of the vagina and the vaginal portion of the cervix. They stressed the vulnerability of these sites and stated that the gonococci penetrate deeply into the tissue. The vestibule and vagina were mildly affected. Macroscopically the vagina appeared edematous, and there were scattered erosions. The microscopic examination showed excessive desquamation, dilatation of the blood vessels and a cellular

infiltration almost exclusively lymphoid in character in the subepithelial tissues. The infiltrate contained many lymphocytes, some histiocytes and a few plasma cells. Polymorphonuclear leukocytes and eosinophils were absent. The microscopic changes in the vestibule and vagina were mild and principally of focal character; that is, they were histologic inflammatory changes which were on the surface and not subepithelial. This fact led the authors to believe the change may have been due to the local treatment.

In one of Santalow and Nowotelnowa's cases of chronic gonorrheal vaginitis a giant cell metamorphosis occurred in the cylinder epithelium of the cervix and cervical glands as well as in the vaginal portion of the cervix and in the vault of the vagina. They assumed this to be a manifestation of degeneration or to be due to a reaction to the intensive local treatment which this child had received. They cited Hergenberg and Gruner as also having found a giant cell metamorphosis in 1 case.

In 3 of their cases the portiovaginalis of the cervix revealed histologic inflammatory changes in the cylinder epithelium, in the form of marked degeneration with occasional desquamation and perivascular infiltration. These changes were slight in comparison with the inflammatory changes in the vaginal vault and the vaginal portion of the cervix. In the remainder (6) of their cases the epithelial changes ceased at the portion where the stratified squamous epithelium transcends to the cylinder epithelium of the neck. Therefore, they stated that the infection is by direct extension and not via the blood or the lymphatic system. They expressed the belief also that the cervical mucous plug prevents the extension which occurs in adult females. Consequently, they stressed the importance of avoiding intensive local treatment in children. Kenessey, on the other hand, performed autopsies on 2 children, one 14 and the other 10 months old, and found that the gonococcic infection not only spread to the uterus but produced pathologic changes in the ovary and the peritoneum surrounding the uterus. He stated the belief that this indicates a spread of infection via the lymph paths.

Reichert and his associates found that the cervix was involved in 98 per cent of their cases and described their vaginoscopic findings as follows: In the acute stages of the disease the cervix was red and edematous and often was eroded, granular or covered with a pseudomembrane. Occasionally submucous hemorrhages were seen. In the subacute and chronic stages the cervix usually remained large and pedunculated and had deep, irregular crypts in its surface which resembled the distorted cervical os. Occasional atrophic changes were seen during the chronic stage of gonorrheal vaginitis. At the time of puberty the cervix resumed its normal size and appearance. Benson, Steer and Speer mentioned that the vaginal rugae may be continued onto the vaginal surface of the cervix so as to make the cervix appear

lobulated. This condition can easily be incorrectly interpreted in vaginoscopic examinations as a pathologic change due to gonococci. Further, they stated the belief that involvement of these rugae on the vaginal surface of the cervix does not indicate endocervicitis. Te Linde (1938 a) in his 175 cases found the essential condition to be vaginitis and only the vaginal portion of the cervix, not the endocervix, to be involved. Brunet found that 80 to 96 per cent of his patients had endocervicitis.

In the rectum inflammatory changes occurred from the transitional fold of the skin to the rectal mucosa in 3 of 6 patients examined by Santalow and Nowotelnowa. In 3 of their patients histologic inflammatory changes occurred in the anterior portion of the urethra. In 3 normal children of the same ages whom they examined as controls, these changes were not present.

The Bartholin glands are rarely involved, as they are undeveloped rudimentary gland structures in children.

Burpee, Robinow and Leslie performed an autopsy on a child who had gonorrheal vaginitis and who died of heart disease. She had received 40,000 units of estrogenic substance over a period of forty days, and no deviations from normal were noted. Miller reported that ovarian tissue removed for biopsy from a patient treated with estrogenic substance was normal. Adler, Steer and Weinstock also reported an autopsy on a 10 year old patient who received 30,000 international units of estrogenic substance in thirty days and who died from streptococcic peritonitis. The tubes, the uterus and the ovaries were considered normal.

COMPLICATIONS

The incidence of complications in a total of 1,232 cases was summed up from the reports of the following authors: Lewis and Adler (1937); Wilde and Wolf; Reichert and his associates; Burpee, Robinow and Leslie; Cohn; Te Linde (1938a); Saxl; Hoeppner Dutra; Schauffler, Kanzler and Schauffler; Gibson and Wiley; Chosson; King, and the London County Council. The results of the summary were as follows:

	No. of cases
Urethritis	439
Proctitis	236
Arthritis	8
Tubal infection	14
Ophthalmia	8
Pelvic peritonitis	6
General peritonitis	67
Septicemia	3
Urethral ducts	2
Inflammation of the navel	1
Otitis media	1

Relation of Forms of Treatment to Recurrence in Cases of Gonorrheal Vaginitis in Children

Author	Number of Patients Treated	No. of Patients Apparently Cured	Number of Recurrences	Treatment
Lewis and Adler.....	82	80	25	Amniotin suppositories (1,000 international units) inserted daily in the vagina
Mazer and Israel.....	60	60	5	Hypodermic injections of 1,000 to 1,500 rat units of estradiol benzoate every other day for eight weeks
	9	9	4	Hypodermic injections of 1,000 to 1,500 rat units of estradiol benzoate for four or five weeks
	18	18	6	Injections of 500 rat units of estradiol benzoate every other day for five to eight weeks
	6	6	3	Estradiol (progynon DH) 1,500 rat units orally twice daily for eight weeks
Little.....	39	19	1	Special hydrolyzed dextrose tablets, 1 tablet inserted in the vagina twice daily, plus occasional douches with saline solution and douches with a 2 per cent solution of lactic acid once a week
Te Linde.....	175	175	2*	Amniotin suppositories (1,000 international units) inserted in the vagina daily at bedtime
	17	12	5	Floraquin suppositories (containing 0.1 Gm. of diodoquin, lactose, dextrose and boric acid) inserted two or three times daily into the vagina for from 35 to 123 days
Burpee, Robinow and Leslie	47	41	5	Estrone (theelin) in oil (2,000 international units) given intramuscularly three times weekly
	8	7	2	Estrone (theelin) in oil (2,000 international units) given intramuscularly three times weekly plus fever therapy (typhoid vaccine by intravenous injection and treatment with the Kettering hypertherm)
	19	8	1	Intravenous injection of typhoid vaccine (Lilly) and in 5 cases treatment with the Kettering hypertherm
	22	11	1	Sulfanilamide orally, 5 grains (0.32 Gm.) per 20 pounds (9.1 Kg.) of body weight, given three times a day for two days, after which 2½ grains (0.16 Gm.) per 20 pounds of body weight was given three times a day for five or more days
	8	2	1	Combination of sulfanilamide and fever therapy
Wilde and Wolf.....	7	7	4	Folliculin menformon (Degewop), 10,000 units given intramuscularly on the first day; on the following days 1,000 units given orally four times daily until a negative vaginal smear was obtained (this treatment given along with local douches); then 1,000 units given orally three times daily without local treatment for two or three weeks
Jess.....	19	19	8	Estradiol benzoate (progynon B) by intramuscular injection, total amount ranging between 10,000 and 250,000 rat units in from two weeks to three months
Toegel.....	10	10	4	Folliculin menformon (Degewop), daily intramuscular injections (1,000 to 10,000 rat units), plus local treatment with silver preparations
Volavsek.....	12	12	4	Folliculin menformon (Degewop), initial intramuscular injection of 10,000 units, followed by oral administration of 1,000 units four times daily until a negative vaginal smear is obtained; then 1,000 units three times daily for three weeks (a thorough local treatment is given throughout the course)

Relation of Forms of Treatment to Recurrence in Cases of Gonorrheal Vaginitis in Children—Continued

Author	Number of Patients Treated	No. of Patients Apparently Cured	Number of Recurrences	Treatment
Reichert, Epstein, Jung and Colwell	71	40	2	Local treatment only (mercurochrome, merthiolate, lactic acid, strong protein silver and metaphen); the recurrences were those treated with mercurochrome and lactic acid, respectively
	32	24	5	Estrone (theelin) in oil and in aqueous solution and placental extract, the total amount ranging from 500 to 6,000 rat units
Berry	25	24	7	Estrone (theelin, Parke, Davis & Company) injections; total dosage averaging from 12,000 international units in the acute cases to an average of 8,500 in the mild cases
Holmes, Jones and Gildersleeve	30	27	9†	Silver picrate suppositories (each contains 1 grain [0.06 Gm.] of silver picrate)
Limper and Hieronymus	4‡	4	2	Ethylene glycol solution of amniotin, 50 to 100 rat units given subcutaneously three times a week
Total	720	615	106	

* The two recurrences were from a follow-up study of the first 100 cured patients. The follow-up was from two months to two and one-half years.

† Twenty patients were followed up for six months. The other ten were not followed for a full six months.

‡ Twenty-seven patients were treated with intramuscular injections of amniotin in oil, estradiol benzoate (progynon B) in oil and folliculin menformon. Twenty-four were cured.

There appears to be an increase in the incidence of complications during the past few years. This may be due to a more thorough study of the children, since it does not appear from the survey of the literature that an increase in the severity of the disease has taken place.

INCIDENCE OF PROCTITIS AND URETHRITIS

There is still considerable difference of opinion as to the incidence of proctitis and urethritis occurring in children suffering from gonorrheal vaginitis (Te Linde [1938 a]; Lewis and Adler [1936]; Santalow and Nowotelnowa; Schauffler, Kanzler and Schauffler). At the Metropolitan Hospital no symptoms or signs of proctitis have been seen even in children who had positive rectal cultures.

RECURRENCE

Several theories have been suggested to explain the recurrences found by the authors listed in the accompanying table. Berry expressed the opinion that a focus of infection in the region of the cervix is responsible. Benson suggested that the persistence of rectal infection may result in a recurrence. The question of recurrence and reinfection is not at all settled. Benson suggested that one should suspect reinfection rather than

recurrence when a child thought to be cured is discharged to infected parents and again shows signs of vaginitis. Burpee, Robinow and Leslie expressed the belief that reinfection is the most common cause of recurrence.

CRITERIA OF CURE

It is becoming more and more evident that the criteria of cure formerly accepted are now considered unsatisfactory. There is a definite tendency to insist on negative cultures before declaring that a child is cured. The London County Council suggested that four months of observation with smears and cultures after cessation of all treatment should pass before a child is considered cured.

PROVOCATIVES

A long list of provocatives have been suggested in the literature in the hope that some aid might be found in determining a cure. However, none of the authors appears to be satisfied. This is an important field for further investigation.

DIAGNOSIS

Owing to the frequency of nongonorrheal vaginitis, the question of diagnosis is one of extreme importance. In a large proportion of the reported cases of vaginitis in children the condition has been diagnosed on the basis of smears. Recent studies have revealed that the use of smears only is not reliable enough and that examination should include cultures. Rorke found that the use of cultures was essential at the Royal Free Hospital. He reported the following data in 1937: 517 cases in which both smears and cultures were positive; 31 cases in which smears were positive and cultures negative; 323 cases in which smears were negative and cultures positive.

Carpenter and Leahy examined 843 cultures and smears from 245 patients seen over a period of three years. There were 223 instances of positive findings by both smear and culture. Positive cultures were obtained in 205 instances (91.93 per cent of the total positive findings) and positive smears in 107 (48 per cent), the greater superiority of the culture method thus being shown.

At a round table discussion the advisory council of the Milbank Memorial Fund agreed that stained smears were particularly subject to error and were positive in only half of those cases of infection in women in which cultures were positive. However, as there are at present a definite proportion (8 per cent) of instances in which positive smears are obtained with consistently negative cultures, it was emphasized that in diagnosis the two technics must be used together rather than one to the exclusion of the other.

Kaplan and Wolfram, Spohr and Landy, Carpenter and Leahy, Cohn, Benson and others have compared the culture method of diagnosis with the smear method. The consensus is that culture has a definite superiority over smear in demonstrating the presence of gonococci but that both should be used. The presence in vaginal smears of gram-negative diplococci other than gonococci has been shown by various authors. Cohn described 2 instances in which the organisms seen on smear were proved by culture not to be gonococci. Coutts and Donoso Barthet cultured the cervical secretion from 20 prostitutes who had a history of having practiced buccal coitus. Two cultures of gram-negative diplococci were obtained, and both were identified as belonging to the Diplococcus pharyngeus flavus group. Skomorovskaia exposed different strains of Staphylococcus aureus to the influence of urine, age and blood serum. After about ten days he found that these bacteria on culture and smear became gram-negative and had a morphologic appearance similar to that of gonococci.

The advisory council of the Milbank Memorial Fund has stated that the complement fixation test has not as yet been perfected to such a degree that it can be used as a routine laboratory procedure. A more specific antigen is still to be discovered and therefore is an important subject for special study.

TREATMENT

Since the last review in 1936 new methods of treatment for gonorrheal vaginitis have been instituted. The literature reveals that there is no single method of treatment that is entirely satisfactory. Since most authors have different criteria of cure it is difficult to evaluate the results of the different forms of treatment.

It is generally agreed that the general treatment is paramount in all cases and that every measure should be taken to increase the resistance to infection and to build up the general health of the child.

The survey on the use of local applications with antiseptic substances as a form of treatment has shown it to be unsatisfactory (Schauffler, Kanzler and Schauffler; Häberlin; Brown). Kobak and Frankenthal, on the other hand, had good results with daily vaginal insertions of silver picrate suppositories (1 grain [0.06 Gm.]).

The administration, action and effects of estrogenic substance have been delved into more deeply (Mazer and Schechter). Such substance has been accepted by many investigators (Te Linde, 1938 b) as the best form of treatment. Its action is based on two factors: (1) It increases the number of layers of epithelial cells of the vaginal mucosa; (2) it causes the vaginal secretion to become strongly acid, with the p_H dropping to 5 or below (Lewis and Adler, 1936). The vaginal response to estrogen usually occurs in two weeks and lasts four weeks after cessation of treatment (Te Linde, 1938 a).

Te Linde (1938 a) has shown that estrone (theelin) in ethylene glycol solution is not effective but that the use of other vehicles produces the desired vaginal changes. This fact probably explains the poor results obtained by Witherspoon and others.

Lewis and Adler (1937), Te Linde (1938 a) and others have used different routes of administering amniotin, namely, the oral, the hypodermic, the intramuscular and the vaginal. The best results were obtained with the use of vaginal suppositories containing 400 to 800 international units. It was determined that a daily dose of 800 international units was as effective as larger doses (Te Linde, 1938 a).

Te Linde (1938 a) treated 159 patients with amniotin suppositories and obtained 159 cures in an average time of seventeen and eight-tenths days. He followed up 100 of the 159 from three months to two and a half years. Ninety-eight of them are well.

The advantages of treatment with estrogenic substance, according to Lewis and Adler (1936), Benson, Te Linde (1938 a), Schauffler, Kanzler and Schauffler and others, are (1) that it is efficient, (2) that its action is rapid, (3) that the technic is simple, (4) that it may be used at home and (5) that there is apparently no harmful effect. The disadvantages reported are (1) that it has undesired effects on other parts of the body and (2) that there is a high incidence of recurrence. Among the undesired effects are swelling of the breasts, growth of pubic hair, swelling of the labia and occasionally uterine bleeding and abdominal pain as a result of congestion of the ovaries, uterus and tubes (Schirner; Toegel; Limper and Hieronymus; Mazer and Schechter; Jess; Reichert and his associates, and Wilder and Wolf). As mentioned earlier in this paper, although generalized effects may be associated with treatment with estrogenic substance no harmful effects can be found at autopsy. Furthermore, any undesired effects which may occur always disappear with the cessation of treatment, if not sooner. Adler, Steer and Weinstock could find no evidence that treatment with estrogenic substance had any influence on growth and development in children 8 years of age or older who were followed for two and a half years.

Estrogenic substance combined with local treatment has been used by many authors with good results (Hohorst and Gassman; Volavsek; Reichert and his associates; Berry; Schauffler, Kanzler and Schauffler, and Schirner). Some of the advantages of combining estrogen with various chemicals are that cervicitis, which is the most frequent cause of recurrence, is treated locally and that more patients are cured than is possible with estrogenic substance alone.

Since some authors assume that it is the lowering of the p_H of the vaginal secretion which produces the therapeutic effect of estrogenic substance (Little), Karnaky attempted to prove the assumption by using acids and acidulated tablets. The results were doubtful.

Other forms of treatment, including fever therapy, have also been reported, but startling results have not been produced.

Sulfanilamide has been used in gonorrheal vaginitis by many investigators. There is a wide divergence of opinion as to the effectiveness of this drug, possibly because different doses were used by the various authors or because of variations in the duration, method or intensiveness of treatment or in the criteria of cure. The percentage of cures reported by the various authors varies from 19 to 100. Since many factors are involved, it is difficult to evaluate these results. In spite of the disadvantages described, such as toxic reactions and the care required in observing the patients, it would appear that a certain number respond dramatically to sulfanilamide. If such cures occur they are found during the first two weeks of treatment, while if failures occur repetition of treatment will not produce results. The final word has yet to be said as to the value of sulfanilamide and its derivatives in the treatment of gonorrheal vaginitis.

In the previous survey problems which required solution were listed. The literature of the last few years has added little toward the solution of those problems. The outstanding problem still remains "the formation of criteria for the diagnosis and cure of vaginitis which would be generally accepted."

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News and Comment

UNIVERSITY NEWS

University of Michigan.—Dr. Charles F. McKhann, of the department of pediatrics of Harvard Medical School, has been made professor of pediatrics and communicable diseases and chairman of the department of pediatrics and communicable diseases at the University of Michigan. He will assume his duties Sept. 1, 1940.

PERSONAL NEWS

Dr. Charles K. Johnson Retiring.—Dr. Charles K. Johnson, professor of pediatrics at the University of Vermont, is retiring after forty-one years in practice. Dr. Johnson is the dean of pediatricians in his state and is very much beloved.

Dr. Alan Brown Honored.—Dr. Alan Brown, professor of pediatrics, University of Toronto, has been made an honorary fellow of the Royal College of Physicians. He is also to give the Blackader Oration before the Canadian Medical Association this year.

DEATHS

Dr. Bernard Fantus, for many years interested in therapy for children, died recently in Chicago. He was best known with respect to his efforts to make food and drugs, such as cod liver oil, palatable for children. He was an associate fellow of the American Academy of Pediatrics.

Obituaries

GLENN E. CULLEN, PH.D.

1890-1940

The death of Glenn E. Cullen means much more than bereavement to his family and friends; there is a great loss to science in general and pediatrics in particular. Dr. Cullen was the first active member of the American Pediatric Society who did not hold the degree of Doctor of Medicine. He was also an associate fellow of the American Academy of Pediatrics. These associations were in addition to his membership in many other scientific organizations and constituted recognition of the fact that his fine knowledge of biochemistry and of the principles and methods of research was vigorously applied to the problems of pediatrics. It was almost uncanny how his knowledge of fundamental science and his continued interest in contributing to it could be transferred to the clinic. Many times in discussion and on rounds his clinical sense amazed his colleagues, and it was a favorite quip of his that he was "almost as good as the pediatrician." His many accomplishments in science will be detailed elsewhere, but it should be noted here that he was, at the time of his death, professor of pediatric research in the University of Cincinnati, College of Medicine, professor of biochemistry in the graduate school of the University of Cincinnati and director of laboratories in the Children's Hospital Research Foundation.

All who knew Dr. Cullen have a keen realization that they have lost a most helpful friend in addition to a colleague.

A. G. M., M.D.

Abstracts from Current Literature

Biochemistry, Bacteriology, and Pathology

A Cultural Study of Filamentous Bacteria Obtained from the Human Mouth. B. G. Bibby and G. P. Berry, J. Bact. **38**:263 (Sept.) 1939.

By the use of anaerobic methods and a wide variety of culture mediums, the authors have isolated a large number of strains of filamentous bacteria from the mouth. On the basis of a study of the appearance and of the characteristics of growth of the 83 strains which were successfully carried in subculture, a tentative working division into seven groups is proposed. Of these, six groups have distinct characteristics. Only two, however, can be identified with organisms which have been isolated by previous investigators, although a third group shows some resemblance to organisms that have been described. Four of the groups of filamentous organisms have the characteristics of the genus Leptotrichia, one those of the genus Fusiformis and one those of both genera. Of all the groups, only one embraced strains all of which were alike in biologic properties. For these organisms the authors suggest the name Leptotrichia buccalis, because they represent the most commonly isolated of the culturable oral filaments.

Stoesser, Minneapolis.

Studies on Lactobacilli: I. Fermentation Reactions of Strains Isolated from Human Mouths. R. W. Harrison, J. Infect. Dis. **65**:142 (Sept.-Oct.) 1939.

Lactobacilli isolated from patients with various degrees of active dental caries were studied in milk and in ten carbohydrates. Of 111 strains in three morphologic groups, 101 were allocated to two main groups on the basis of activity in milk and to nine subgroups, determined from their action on four carbohydrates. There was little correspondence between morphologic and fermentative properties.

Toomey, Cleveland.

Megalomorphic Phase of Bacteria. J. G. Wahlin and P. J. Almaden, J. Infect. Dis. **65**:147 (Sept.-Oct.) 1939.

The existence of large forms of bacteria has been confirmed, and the term "megalomorph" has been used to designate them.

Megalomorphism has been studed in the following species: Eberthella typhosa; Shigella paradysenteriae, Flexner and Sonne strains; Salmonella paratyphi; Salmonella schottmülleri; Brucella abortus; Brucella suis; Alcaligenes faecalis; Escherichia communior; Aerobacter aerogenes; Aerobacter oxytocum; Klebsiella pneumoniae; Klebsiella ozaenae; Serratia marcescens.

In all the cultures studied the development of megalomorphs was preceded by filament formation, characteristic of the R phase. In many instances a subsequent reversion to the S form occurred.

The mode of origin of the megalomorphs varies, and this gives rise to structures of several types.

The megalomorph is not an involution form but represents a stage in the life cycle of bacteria.

Toomey, Cleveland.

Filtrability and Morphologic Changes of Bacteria of the Typhoid Group. W. Schmidt-Lange and W. Hepp, Arch. f. Hyg. **121**:209 (Jan.-Feb.) 1939.

The authors investigate the question of the existence of a filtrable virus in the typhoid bacilli group. They employed for filtration of the cultures membrane filters composed exclusively of cellulose esters, which act as a sieve of uniform pores, and they used mediums of lithium chloride and crystal violet agar.

It was not possible to grow bacteria from filtrates through membrane filters having a maximal pore diameter of 0.3 micron; and there was no indication of virus formation in cultures to which a bacteriophage had been added.

By observation of living cultures of Bacterium breslaviense and Bacterium typhi in a thermostat microscope, all stages of transformation of the small rods into fine granules could be confirmed, the granules being a form of the bacteria which may pass occasionally through even fine-pored filters.

FALKENHEIM, Rochester, N. Y.

Metabolism; Infant Feeding; Milk and Other Foods

INTRAVENOUS FEEDING OF AMINO ACIDS. I. CORBOULD, R. H. CLARK and R. E. McKECHNIE II, Am. J. Digest. Dis. **6**:185 (May) 1939.

This study shows that rabbits fed intravenously or intraperitoneally on a mixture of amino acids from hydrolyzed casein, supplemented with tryptophane and vitamin A, lose practically no weight over a period of two weeks and remain in normal physical condition. Rabbits fed only dextrose lost weight slowly after the first few days. When amino acids as well as dextrose were given intravenously, the loss of weight was slower. When tryptophane was added, the loss of weight did not occur for one week. When vitamin A was added, the period before loss of weight occurred was lengthened.

MORRISON, Savannah, Ga.

CLINICAL STUDIES IN ACIDOSIS AND ALKALOSIS; USE AND ABUSE OF ALKALI IN STATES OF BICARBONATE DEFICIENCY DUE TO RENAL ACIDOSIS AND SULFANILAMIDE ALKALOSIS. A. F. HARTMANN, Ann. Int. Med. **13**:940 (Dec.) 1939.

This article can be abstracted best by quoting the author's summary and conclusions.

"1. Plasma $BHCO_3$ reduction in chronic nephritis and other forms of renal insufficiency may occur with the production of a real acidosis of the 'metabolic type' without abnormal acid retention, due fundamentally to inadequate reabsorption by the tubules of $BHCO_3$ from the glomerular filtrate.

"2. Severe and persistent acidosis has been noted in an infant of four months in whom the only demonstrable renal lesion seems to be failure of the tubules to reabsorb $BHCO_3$.

"3. There is a logical use for the administration of alkali, particularly as sodium *r*-lactate, in such cases, both to relieve and prevent recurrence of significant degrees of acidosis.

"4. Plasma $BHCO_3$ reduction which follows sulfanilamide administration, on the other hand, must be looked on as compensatory for a primary carbon dioxide deficit alkalosis.

"5. There is no logical reason for the routine use of alkali with sulfanilamide to 'prevent acidosis.'"

BOYD READING, Galveston, Texas.

SOME PRACTICAL POINTS IN THE FEEDING OF HEALTHY INFANTS. M. WITKIN, Arch. Pediat. **56**:452 (July) 1939.

Witkin outlines practical points in the technic of breast and bottle feeding.

ORR, Buffalo.

UNIFICATION OF STATISTICS ON BREAST FEEDING. G. FEDDERS, Jahrb. f. Kinderh. **148**:149 (Dec.) 1936.

Of 2,707 infants studied, 48, or 1.7 per cent, were artificially fed; 87.1 per cent were breast fed at the end of one month; 19.1 per cent were exclusively breast fed at the end of six months. Of the 2,707 infants, 1,302 were either exclusively or partially breast fed at the end of six months. The author feels that this is an excellent result.

LANDAU, Hannibal, Mo.

STUDIES WITH HEATED BREAST MILK. H. K. BIRMELE, Monatschr. f. Kinderh. **78**: 201 (May) 1939.

Studies showed that heating breast milk for two minutes at 74 C. destroys the lipase. Fluoroscopic studies, however, showed that there is no delay in the emptying time of the stomach. These studies were made on premature infants.

GERSTLEY, Chicago.

TREATMENT OF PREMATURE INFANTS WITH MODIFIED BREAST MILK. H. KOHL, Monatschr. f. Kinderh. **78**:211 (May) 1939.

In a study of 31 premature infants it was found that the addition of 2 per cent gelatin (aminoacetic acid, lysin and arginine) to the breast milk led to a definite gain in weight. The addition of 2 per cent carbohydrate had no such effect.

GERSTLEY, Chicago.

FAT CONTENT OF HUMAN MILK. U. S. RUZICIC and Z. POPOVIC, Monatschr. f. Kinderh. **80**:135, 1939.

This is a continuation of studies on the effect of frequency of nursing on the fat content of milk. Observations on 10 wetnurses showed that pauses between nursings of from one to six hours had no effect on the fat content of the milk.

GERSTLEY, Chicago.

INFLUENCE OF CURTAILMENT OF THE LENGTH OF NURSING TIME ON THE GASTRIC FUNCTION OF BREAST-FED AND BOTTLE-FED INFANTS. A. YLPPÖ, Acta pædiat. **24**:258, 1939.

Studies of the rate of imbibition were made by weighing 60 healthy infants, some breast-fed and some bottle-fed, at intervals of from two to five minutes during the course of nursing. In this way it was demonstrated that the greatest part of the feeding was consumed during the first two to five minutes and that little air was swallowed during this time. Roentgen examination showed that nursing continued beyond this point resulted in distending the stomach with air and was sometimes followed by evidence of discomfort on the part of the infant until eructation occurred. Significant amounts of air were swallowed only when some fluid remained to be drunk. Sucking on a nipple unattached to a bottle was not accompanied by deglutition; hence, little air was swallowed. In order to permit consumption of the milk within five minutes, the hole in the nipple must be 2 mm. in diameter. For the last year or two Ylppö's clinic has limited the time of breast feeding of healthy infants to ten minutes and the time of bottle feeding to six minutes. No difficulties have arisen as the result of this policy, and it has effected a substantial saving of time for the nursing personnel.

McCUNE, New York.

FRUIT JUICE FOR BREAST-FED CHILDREN—IS IT NECESSARY OR INJURIOUS? C. GYLLENSWÄRD, Acta pædiat. **24**:348, 1939.

Gyllenswärd recognizes serious objections to the common practice of adding fruit juice to the diet of breast-fed infants at the end of the first or second month of life. Popular confidence in the value of breast milk is weakened; the pleasant taste of the juice may diminish the infant's enthusiasm for the breast; digestive disturbances are sometimes produced, and occasionally allergic disorders are provoked. The more logical method of avoiding a deficiency of vitamin C in the infant is to include the substance in the diet of the lactating mother; in this way, both mother and child benefit by the addition.

Over a period of five years a systematic study was made of the effect of supplementing the diet of 37 breast-fed infants with 1 or 2 teaspoons of fresh orange juice daily; 38 infants served as controls. The infants who received orange

juice gained no better than those receiving breast milk alone; their stools were somewhat more numerous, and a few had dermatoses that were thought to be due to the supplement.

McCUNE, New York.

ARTIFICIAL FEEDING OF INFANTS OVER SIX MONTHS OF AGE. A. COLLETT, Acta pædiat. **24**:431, 1939.

In these remarks Collett advises Swedish physicians to adopt dietary practices that are already well established in the United States.

McCUNE, New York.

Vitamins; Avitaminoses

RACHITIC STUDIES: I. DETAILS AND PROCEDURE EMPLOYED IN ANTIRACHITIC TREATMENT. EARL W. MAY and THELMA M. WYGANT, Arch. Pediat. **56**:274 (May) 1939.

This is the first of a series of articles dealing with the subject. In this article the authors discuss their plan of study.

ORR, Buffalo.

STUDIES IN VITAMIN A: RELATION OF VITAMIN A AND CAROTENE TO SERUM LIPIDS. HUGH W. JOSEPHS, Bull. Johns Hopkins Hosp. **65**:112 (July) 1939.

A series of observations has been made correlating the levels of vitamin A, carotene, cholesterol and fat in the blood as part of a study to determine the factors which must be considered in an interpretation of the vitamin A content of the blood. The only conclusion to be drawn is that there is an obvious relation between vitamin A, carotene and the total lipid content of the blood, and it is suggested that the basis for this is the fat solubility of vitamin A and carotene. It is not possible at present to conclude that the concentration of vitamin A in the fat of the plasma is more significant than the concentration in the plasma itself, though certain observations discussed in the article indicate that this is a possibility. The bearing of this relation on interpretation of some of the phenomena observed in previous studies of vitamin A is pointed out.

FROM THE AUTHOR'S SUMMARY.

VITAMINE A WITH SPECIAL REFERENCE TO THERAPY. ARTHUR M. YUDKIN, Bull. New York Acad. Med. **15**:406 (June) 1939.

This is a condensed summary of the present knowledge of this important food accessory and its special therapeutic indications. The author concludes with this sentence: "Although great progress has been made, with a continuation of research, we may confidently look forward to greater advances in our knowledge in this field."

JAHR, Omaha.

A QUANTITATIVE BIOLOGICAL ASSAY OF VITAMIN K. S. ANSBACHER, J. Nutrition **17**:303 (April) 1939.

The author, by experiments on 4,321 chicks, made a comparative study of various basal diets for vitamin K assays. He fed a ration (see K—1 in the original) which caused a severe vitamin K deficiency (a definite hemorrhagic diathesis with prolonged blood clotting time) within fifteen days. When this hemorrhagic syndrome developed, the chick was given the test substance orally for its assay of vitamin K. If vitamin K was present, the clotting power of the blood was restored to normal within a very short time. Ansbacher defines the unit of vitamin K as "the minimal amount necessary to render the blood clotting time of the vitamin K-deficient chick, weighing 70-100 Gms., normal within 6 hours after administration." This unit was found to equal 20 Dam units of vitamin K.

In a footnote (p. 306) he adds that in 100 chicks fed the aforementioned ration the hemorrhagic diathesis failed to develop in the fifteen day period. Enlarged thyroid glands were discovered. Experiments are now under way to demonstrate a relation of the endocrine glands to vitamin K metabolism.

FREDEEN, Kansas City, Mo.

A STUDY OF RACHITOGENIC DIETS COMPOSED OF PURIFIED FOOD MATERIALS. JAMES H. JONES, J. Nutrition **17**:601 (June) 1939.

Jones presented data showing a number of low phosphorus diets, composed of purified food substances, which proved to be rachitogenic for rats. The protein in most of the diets was blood fibrin. Casein, with its large amount of phosphorus, if fed at a level of not over 12 per cent produced a fair degree of rickets. In diets containing 3 per cent calcium carbonate the level of available phosphorus had to be lower than 0.1 per cent to produce severe rickets. The author suggested that these diets may be used to advantage in the assay of materials for the vitamin D content.

FREDEEN, Kansas City, Mo.

TREATMENT OF RICKETS AND TETANY WITH A SINGLE MASSIVE DOSE OF VITAMIN D: VITAMIN D SHOCK THERAPY. HERMANN VOLLMER, J. Pediat. **14**:491 (April) 1939.

Three infants, one 6 months of age and suffering from rickets, the other 2 aged 12 days and 5 months, respectively, and suffering from tetany, with low levels of serum calcium, were treated with 600,000 units of vitamin D by mouth in one dose. Striking results have been obtained with vitamin D shock therapy. One to three days after this massive therapy a child with rickets becomes happy and active. The level of blood phosphorus may return to normal as early as four days after treatment, and calcification in the long bones occurs soon after treatment. In the case reported, advanced ossification was seen on the roentgenogram by the twelfth day. In infantile tetany without any treatment other than this single massive dose of vitamin D the convulsions cease, the signs of mechanical hyperirritability disappear within two days and the level of serum calcium rises extremely rapidly. Vollmer, after surveying the literature, states the belief that this massive use of vitamin D is indicated in cases of neonatal and infantile tetany, severe rickets, pneumonia or pertussis associated with rickets and indifference or unreliability of the parents of a rachitic or tetanic child. There are no contraindications to the use of large doses.

RAUH, Cincinnati.

VITAMIN D THERAPY IN CHILDREN. J. M. LEWIS, M. Clin. North America **23**: 687 (May) 1939.

This paper is an appraisal of the value of the various antirachitic agents in common use, with suggestions as to the effective dosage and the technic of administration.

SMITH, Ogden, Utah.

THE GASTROINTESTINAL ASPECTS OF DEFICIENCY DISEASE. JULIUS FRIEDENWALD and SAMUEL MORRISON, West Virginia M. J. **35**:267 (June) 1939.

Vitamins are as important to health as are other food elements. Although knowledge of the subject is far from adequate, one is able to present fairly comprehensive pictures of many problems of avitaminosis.

There is a close relation between deficiency diseases and the gastrointestinal tract.

Pernicious anemia and other anemias, polyneuritis and pellagra are largely if not entirely due to deficiency states resulting from disturbances of the digestive tract.

Vitamins A, B_1, B_2, C, D and K in relation to disturbances of the gastrointestinal tract are discussed at length.

The relation between gastrointestinal disturbances and deficiency diseases may be reciprocal.

Further study is required.

In the treatment of gastrointestinal conditions the possible presence of vitamin deficiencies as etiologic factors must be kept constantly in mind.

SHAWKEY, Charleston, W. Va.

TESTS FOR VITAMIN C DEFICIENCY IN CHILDREN OF SCHOOL AGE. NEIMANN and DEDUN, Rev. franç. de pédiat. **14**:253, 1938.

Neimann and Dedun review the various tests for vitamin C deficiency. They chose from these, for their clinical study of 207 children, the two most suitable ones. The first is that of Goethlin, in which a count is made of the number of petechiae developing as a result of partial obstruction of the venous return in the arm. This is carried out by the use of a blood pressure cuff maintained at 50 mm. of mercury for fifteen minutes. A count of over 5 is said to indicate vitamin C deficiency. The second test is that of Tillmans, in which the vitamin C content of the urine is measured. A value of under 1 mg. in 100 cc. is said to indicate deficiency. Only 9 children showed urinary ascorbic acid under 1 mg. in 100 cc., whereas 40 had over 5 petechiae. The authors conclude that neither test is absolute but that both may serve to indicate children who should be studied further.

LESLIE, Evanston, Ill.

ACUTE INFECTIONS AND THE BLOOD CAROTENOIDS OF INFANTS AND YOUNG CHILDREN. P. LUCIANI, Lattante **10**:302 (July) 1939.

The carotenoid content of the blood of 8 infants and children was only slightly lowered (4 per cent) during an attack of mild influenza (rhinitis and rhinopharyngitis). Measles in 11 children, especially when accompanied by chickenpox, led to a consistent average fall of 33 per cent in the concentration of blood carotenoids. This fall in the level of previtamin A was probably due to lessened food intake, poorer absorption, fever and infection. The normal carotenoid content of the blood of children is 0.05 mg. per hundred cubic centimeters.

HIGGINS, Boston.

TREATMENT OF RACHITIC CHILDREN WITH LARGE DOSES OF VITAMIN D_2. A. MACCHI and F. GIONGO, Med. ital. **20**:218 (May) 1939.

The authors report the result of treating 10 rachitic infants with large doses of vitamin D_2. The infants were 4 to 20 months old. Before treatment each one was examined roentgenographically and the level of calcium and of phosphorus in the blood was determined.

They were given 15 mg. of vitamin D_2 in an oily solution. The roentgen examination and the tests for calcium and phosphorus were repeated every eight days. No other antirachitic therapy was given. The values for calcium and phosphorus are given in a table. Roentgenograms show the initial lesions and the course of healing under vitamin therapy.

The authors conclude that healing can take place in five to six weeks with administration of large doses of vitamin D.

MARTOCCIO, Utica, N. Y.

BLOOD GUANIDINE, CALCIUM AND POTASSIUM IN SPASMOPHILIC INFANTS (PRELIMINARY REPORT). A. DORDI, Med. ital. **20**:418 (Aug.) 1939.

The author studied the values for guanidine, calcium and potassium in the blood in 9 cases of infantile tetany. The value for guanidine was determined by the method of Major and Weber as modified by Minot and Dood. The values during

the period of tetany were between 0.20 and 0.30 mg. The normal values were about the same as during the period of tetany. The value for calcium was from 5.2 to 6.8 mg. The potassium level was normal. The author was interested in determining whether or not the neuromuscular disturbances were caused by an increase in the guanidine content of the blood. MARTOCCIO, Utica, N. Y.

ACTION OF VITAMIN B_1 ON THE PANCREATIC ENZYMATIC ACTIVITY OF CHILDREN. G. PIANA, Riv. di clin. pediat. **37**:353 (April) 1939.

The tryptic, the amylolytic and the lipolytic action of the duodenal juices of 10 normal children between 3 months and 3 years of age were determined before and after the giving of vitamin B_1. Five hundred to 1,000 units of vitamin B_1 was given parenterally each day for ten days. Some increase in tryptic and amylolytic activity and a marked increase in lipolytic activity were observed. This should explain the increased fat tolerance following vitamin B_1 therapy.

HIGGINS, Boston.

COMPLEMENTARY ACTIVITY OF THE SERUM AND VITAMIN C. C. ARDY, Riv. di clin. pediat. **37**:495 (June) 1939.

In observations on guinea pigs, Ardy was able to find no variation in the complement of the blood serum following either a scorbutic diet or administration of large amounts of ascorbic acid. HIGGINS, Boston.

CAROTENOID CONTENT OF THE BLOOD OF NURSING MOTHERS AND CHILDREN. P. LUCIANI, Riv. di clin. pediat. **37**:631 (July) 1939.

The carotenoid content of the blood of nursing mothers averaged 0.037 mg. per hundred cubic centimeters during the first few days of the puerperium and rose to 0.050 mg. after one month of nursing.

The carotenoid content of the blood of infants averaged 0.040 mg. per hundred cubic centimeters in the newborn period, 0.023 mg. in the first semester of life and 0.028 mg. in the second.

Healthy children had an average blood carotenoid content of 0.053 mg. per hundred cubic centimeters, while for children with acute febrile illnesses the average value was only 0.023 mg. HIGGINS, Boston.

RACHITIC HYPOPHOSPHATEMIA AND ULTRAVIOLET IRRADIATION. F. RASI, Riv. di clin. pediat. **37**:692 (Aug.) 1939.

Observations were made on 5 healthy and 8 rachitic infants who had been without food for twelve hours; the blood was withdrawn before and immediately after irradiation with a quartz lamp. Irradiation of the healthy infants caused no consistent increase in the level of phosphate in the blood, but irradiation of the infants with active rickets resulted in consistent appreciable increases.

HIGGINS, Boston.

VITAMIN C CONTENT OF WOMEN'S MILK IN SASSARI. G. MARIA DORE, Riv. di clin. pediat. **37**:769 (Sept.) 1939.

Determinations were made of the ascorbic acid content of the milk of 45 Sardinian mothers. The amount of ascorbic acid tended to be less than that reported for mothers' milk elsewhere. The ascorbic acid content of the milk was highest in May, June and July. The stage of lactation and the type of diet did not consistently affect the vitamin C content of the milk. Parenteral injection of vitamin C distinctly increased the amount in the milk. HIGGINS, Boston.

VITAMIN C METABOLISM IN NORMAL AND SICK CHILDREN. L. F. MEYER and P. ROBINSON, Arch. de pediat. d. Uruguay **11**:1089 (March) 1939.

This interesting work was carried out with 1,400 normal infants and 109 sick children with pneumonia, empyema, diarrhea, pulmonary abscess and toxicosis.

The vitamin C metabolism was studied by determining the urinary output of the vitamin and its concentration in the blood during twenty-four hours, the urinary output being modified by the daily intake of the vitamin.

Figures are given for normal children, varying from 16 to 20 mg. in the cases of infants hospitalized and obtaining a regular diet.

Preschool children required 30 to 45 mg. of vitamin C daily. Children of the poorer classes are said to need the largest amount of vitamin C, calculated as 500 mg. according to the saturation test. By the method used the amount required by children with a high temperature was not found to be increased.

Vitamin C given by mouth to children with diarrhea was not absorbed; consequently the vitamin was not used by the organism except when it was administered parenterally.

The findings in cases of toxicosis were interesting, vitamin C not being used in cases of the most serious involvement. However, improvement was followed by a much better utilization of this vitamin resulting in a good prognosis in these cases.

SOTO, Habana, Cuba.

A CASE OF MOLLER-BARLOW'S DISEASE. P. ORSINI, Med. inf. **10**:105 (April) 1939.

A child aged 13 months who had been breast fed for twelve months had pain in the right shoulder which proved on roentgen examination to be due to a subperiosteal hematoma. A diagnosis of scurvy was made, and the child showed marked improvement after the administration of lemon juice.

HIGGINS, Boston.

Hygiene; Growth and Nutrition; Public Health

DATA ON THE GROWTH OF PUBLIC SCHOOL CHILDREN (FROM THE MATERIALS OF THE HARVARD GROWTH STUDY). W. F. DEARBORN, J. W. M. ROTHNEY and F. K. SHUTTLEWOTH, Monograph of the Society for Research in Child Development, Washington, D. C., National Research Council, 1938, vol. 3, no. 1.

This monograph presents the detail of repeated physical and mental measurements on 747 boys and 806 girls, whose records were selected for completeness of data from among the records of the Harvard study of growth. The age range of the subjects was from 5 to 21 years. Eleven or more sets of annual measurements are available for 1,225 boys and girls. Each set consists of seven physical measurements, counts of erupted teeth and two group intelligence tests. In addition measurements of head width and head length for every other year are available. On many complete series of estimated skeletal ages are to be had, and on all the results of at least one and often four or more Stanford Binet tests. All told, 155,791 physical measurements and 33,837 mental ages are reported. Supplementary data include sex, date of birth, ages at measurement, city, ethnic stock and socioeconomic status. Information concerning the first menstruation is available for about 300 girls. Administrative procedures and technics of measurement are described in detail. An annotated bibliography of 75 studies based on these records is included.

The data thus made available provide materials for a host of minor and major studies. For the first time it will be possible to check and recheck findings. The ingenuity of all students rather than of a favored few can now be exercised in the invention of better methods of analysis. All those who collect important bodies of developmental data are henceforth under obligation to make their mate-

rials available to all. The combined influence of these factors marks the publication of this extensive collection of original data as an important milestone in the field of child development and of human biology.

PALMER, Washington, D. C.

A HANDBOOK OF METHODS FOR THE STUDY OF ADOLESCENT CHILDREN. F. K. SHUTTLEWORTH, Monograph of the Society for Research in Child Development, Washington, D. C., National Research Council, 1938, vol. 3, no. 2.

In this volume five experts have pooled their resources together with the advice and assistance of many specialists in the evaluation of essentially all the existing technics of the life sciences which are suitable for studying the growth and development of adolescents. The result is a critical compendium of methodologies which is important for all who are working with or studying children. Two central themes dominate the volume. First, the important phenomena to be measured are changes, developmental sequences, unfolding patterns, and rates and directions of growth in structures, functions and activities which occur in time. This longitudinal emphasis is opposed to the traditional cross-sectional emphasis in which the purpose of measurement is to assess the capacities of an individual relative to his contemporaries of the same age and sex. Second, the child must be considered as a biologic organism growing in a culture. That is, the many aspects of structure, function, activity and impinging culture must be regarded not as isolated items, to be analyzed as discrete units, but as components in an organized whole that cannot be dismembered without destroying the reality which needs to be studied. This organismic conception is opposed to the traditional conception, which is concerned with the analysis of the causal interaction of two or more isolatable variables and which, while contributing greatly to the understanding of particular aspects of human biology, has contributed little to the understanding of the child as such.

The twenty-five chapters are arranged in five parts, each prepared by one of the five authors. These include chapters on anthropometry, skeletal development, four chapters on the skin, genital changes, blood, respiration and energy metabolism, digestive organs and functions, urine and feces, dentition, circulation, posture, physical fitness tests, sensory phenomena, perception and imagination, motor performances, intelligence and educational achievement, special abilities, measurable aspects of the environment, hereditary and environmental differences, and statistical considerations.

PALMER, Washington, D. C.

THE ADOLESCENT PERIOD: A GRAPHIC AND PICTORIAL ATLAS. F. K. SHUTTLEWORTH, Monograph of the Society for Research in Child Development, Washington, D. C., National Research Council, 1938, vol. 3, no. 3.

This volume, consisting exclusively of graphic and pictorial materials, provides a unique and invaluable supplementary reference for courses in psychology, education, sociology and child development. The 458 charts, including 17 photographs illustrating the process of sexual maturation, present the more important facts concerning every aspect of the second decade of life and much material, in addition, on younger children and adults. Nearly 200 charts are original drawings, and many of these represent distinctive contributions. Each chart carries a brief explanation to insure that the bare facts are correctly understood, a citation of the original source and, when it seems necessary, a few comments on the nature of the original data. The following abbreviated table of contents will suggest the scope of the material.

Introduction: The money value, number, residence, nationality of adolescents, etc. Figures 1 to 7.

Physical Growth and Development: Body size, body volume, dentition, skull and face, ossification, changing proportions, individual differences, increments, seasonal variation, heredity, race, socioeconomic status, etc. Figures 8 to 89.

Sexual Maturation: Individual differences and patterns of sexual development, illustrated with nude photographs of both sexes; age at first menstruation; menstrual intervals; relation to physical growth, physiologic functioning, intelligence and maturity of interests, etc. Figures 90 to 160.

Health: Causes of death, declining mortality rates, morbidity, tuberculosis, syphilis, drug addiction, thyroid enlargement, dental caries, vision, hearing defects, duration of illness, diet, economic factors, etc. Figures 161 to 229.

Intelligence: Mental growth curves; intelligence quotients and biologic, physical, medical, racial, hereditary and environmental factors; gifted children, mental defectives, etc. Figures 230 to 267.

Education: Trends in school attendance, learning curves by age and grade, educational progress, intelligence quotients, etc. Figures 268 to 280.

Special abilities, honesty, collections, plays and games, interests and attitudes, movie attendance, etc. Figures 281 to 322.

Behavior Maladjustments: Personality and conduct problems, juvenile delinquency, insanity, crime, etc. Figures 323 to 370.

Occupations: Preferences, trends, major occupations, relationships to school attendance and marriage, etc. Figures 371 to 392.

Sex Adjustments: Questions, knowledge and experience, masturbation, factors making for happy marriage, marital status, etc. Figures 393 to 420.

Urban Influences: School attendance, gainful occupations, and marital status of adolescents and youth in large and small cities. Figures 421 to 447.

Major Activities: Proportions attending school, gainfully occupied, and married at each age from 10 to 24. Figures 448 to 458. PALMER, Washington, D. C.

SEXUAL MATURATION AND THE SKELETAL GROWTH OF GIRLS AGE SIX TO NINETEEN. F. K. SHUTTLEWORTH, Monograph of the Society for Research in Child Development, Washington, D. C., National Research Council, 1938, vol. 3, no. 5.

This study presents the large contrasts in the skeletal growth patterns of three groups of girls, classified according to age at first menstruation. The original data, which were collected by the workers employed in the Harvard study of growth, consisted of measurements made on roentgenograms of the hand and wrist taken annually over periods of seven to twelve years, on 103 girls. These measurements included two metacarpal lengths, four metacarpal widths, five carpal diameters and the greatest diameter of the radial epiphysis. The findings are presented in forty-one charts and are summarized under eight major generalizations. With slight changes in wording, these generalizations are the same as those presented in an earlier monograph, which concerned 248 girls in eight menarcheal groups, analyzed in respect to standing height, sternal height, sitting height, leg length, iliac diameter, chest breadth, chest depth and body weight (Sexual Maturation and the Physical Growth of Girls Age Six to Nineteen, Monograph of the Society for Research in Child Development, Washington, D. C., National Research Council, 1937, vol. 2, no. 5). PALMER, Washington, D. C.

Newborn

A REVIEW OF 1,012 CASES OF INDUCTION OF LABOR. GILBERT J. SCHWARTZ, Wisconsin M. J. **38**:205 (March) 1939.

These cases are reviewed because of the controversy about the effect and mortality rate among both mothers and children from induction of labor at or near term. Comparison is made with a smaller series of cases (500) of spontaneous labor. The membranes were not ruptured until the presenting part had started to engage and the cervix was soft enough to admit a finger.

Castor oil and quinine were then given with (occasionally) small doses of posterior pituitary. Labor was shortened to only 46 per cent of the time required for the noninduced labors.

The percentage of fetal deaths, including stillbirths, and deaths up to the tenth day for the combined groups was 4.1. For the "induced labor group" it was 0.6 per cent (maternal eclampsia; fetal monstrosity; cord about the fetal neck). There were no prolapsed cords.

The babies born by induced labor showed less loss of weight by the fourth day and had gained better by the ninth day than the babies born by normal delivery.

JANNEY, Wauwatosa, Wis.

FAMILIAL ICTERUS GRAVIS OF THE NEWBORN: TRANSITORY ERYTHROBLASTOSIS, ANASARCA AND DEATH. J. H. MONTLAUR and P. P. LÉVY, Bull. Soc. pédiat. de Paris **36**:673 (Nov.) 1938.

Marked jaundice appeared in an infant, a girl, on the first day of life and persisted until she died on the fourth day. Moderate anemia was present. Edema appeared on the third day. A maximum of 1,700 erythroblasts per cubic millimeter was observed in the blood on the second day, after which these cells gradually disappeared. The infant was given injections of blood subcutaneously, intramuscularly and intraperitoneally. The spinal fluid was colored with bile. This was the fifth infant born to the mother. Two previous ones had died of icterus gravis when 4 days old. Although the mother had careful antepartum supervision, which included administration of a proper diet with a high vitamin content and injections of liver extract, this did not prevent the development of icterus gravis in the infant. Anemia accompanying this condition may be severe or moderate, and erythroblastosis may or may not be present. Those conditions are not causally related to the severe jaundice, the cause of which is still unknown.

BENJAMIN, Montreal, Canada.

BIOMETRIC AND STATISTICAL DATA ON ILLEGITIMATE NEWBORN CHILDREN IN THE PROVINCE OF PERUGIA. A. PICCIOLI, Lattante **10**:3 (Jan.) 1939.

In a study of 3,341 newborn infants in the province of Perugia, Italy, 802 were found to be illegitimate—402 boys and 400 girls. The illegitimate infants averaged 4 ounces (113.3 Gm.) less in weight and ¼ inch (0.64 cm.) less in height than the legitimate infants. The illegitimate children of multiparas tended to be heavier and taller than those of primiparas.

HIGGINS, Boston.

PHYSIOLOGIC LOSS OF WEIGHT IN THE NEWBORN. H. RUSCH, Ztschr. f. Geburtsh. u. Gynäk. **119**:1 (May) 1939.

A study of 5,133 normal newborn infants showed an average loss of 3.79 per cent of the birth weight. Four and one-tenth per cent lost less than 4 per cent, and 3.1 per cent lost more than 10 per cent, of the birth weight. Ten per cent is considered the upper limit of normal loss. Insufficient intake of fluid during the first few days is considered the main reason for decrease in weight. Large children lose proportionately more than small ones because of their need for larger amounts of fluid. The average duration of loss of weight was three and forty-nine hundredths days. The amount of weight lost is more significant than the duration of loss.

ADAIR and POTTER, Chicago.

THROMBOSIS OF THE UMBILICAL VEIN IN ONE OF IDENTICAL TWINS. AXEL INGELMAN, Acta obst. et gynec. Scandinav. **20**:8 (Jan.) 1939.

The author gives an account of a case of uniovular twins. One fetus lived; the other was macerated, and death had probably occurred about four weeks before birth. The umbilical vein of the dead fetus contained a recent obturating thrombus, and the umbilical cord was wound twice around the neck. Macroscopic and microscopic examination showed the rest of the body to be normal. The author considers the cause of death unclear. The thrombosis came into existence after death of the fetus by means of the blood circulating from the living fetus.

ADAIR and POTTER, Chicago.

Acute Contagious Diseases

FACTORS INFLUENCING THE INCIDENCE AND COURSE OF OTITIS MEDIA IN SCARLET FEVER. C. WESSELHOEFT, Ann. Int. Med. **12**:1473 (March) 1939.

By a review of the literature Wesselhoeft found reports of 371,788 cases of scarlet fever, in which the incidence of suppurative otitis media was 12 per cent. This coincided with an incidence of 12 per cent in 10,000 cases which occurred on his own service. From a study of data furnished by these cases he concluded that otitis media occurred as a complication of scarlet fever most frequently in patients who were in the first years of life and that it was more frequent in cases occurring in winter. The incidence was not decreased in children whose tonsils had been removed. Paracentesis did not noticeably reduce the incidence of mastoiditis requiring surgical intervention.

Early serum therapy favorably influenced otitis media. The effects of the administration of sulfanilamide as a prophylactic measure against aural complications were not definitely determined.

READING, Galveston, Texas.

BULBAR POLIOMYELITIS FOLLOWING TONSILLECTOMY AND ADENOIDECTOMY. Y. D. KOSKOFF, J. AMSHEL and S. LEBEAU, Arch. Pediat. **56**:19 (Jan.) 1939.

Two cases are reported.

ORR, Buffalo.

DIPHTHERIA: PROPHYLAXIS AND TREATMENT. W. H. FAULKNER, Arch. Pediat. **56**:27 (Jan.) 1939.

The subject is reviewed. Four cases are reported. Three of the patients were treated with antitoxin and sulfanilamide and a fourth with sulfanilamide alone.

ORR, Buffalo.

ERYSIPELAS—A COMPARATIVE ANALYSIS OF SIXTY CASES WITH MASSIVE ULTRAVIOLET IRRADIATION AS AN ADJUVANT IN TREATMENT. H. W. WILLIZ, Arch. Pediat. **56**:39 (Jan.) 1939.

Ultraviolet radiation in massive doses gives promise as an adjuvant to other means of treatment in cases of erysipelas.

ORR, Buffalo.

CONCERNING IMMUNITY AND VACCINATION IN SCARLET FEVER. J. A. KOLMER, Arch. Pediat. **56**:79 (Feb.) 1939.

Scarlet fever is primarily a local infection with hemolytic streptococci belonging to group A of Lancefield capable of producing sufficient erythrotoxin to account for the characteristic exanthem of the disease. In addition to this erythrotoxin, other exogenous toxins may play a role in the genesis of the disease as well as the invasiveness of the streptococci for the fixed tissues and blood.

Probably the local necrotizing effects of the exogenous toxins facilitate or promote the invasiveness of the streptococci of high toxicity and high invasive power. Antitoxic immunity alone may be insufficient for affording protection and thus scarlet fever may be produced among persons possessing sufficient antitoxic immunity for yielding negative skin reactions to the Dick test.

A local infection without the exanthem may occur if the invading streptococci are of low toxicity or if the patient possesses insufficient natural antitoxin or insufficient antitoxin of the type acquired by vaccination with the toxin to prevent occurrence of the characteristic rash. Such infections may and usually do escape clinical detection. They may constitute sources of dissemination of the disease. It therefore seems desirable to produce, if possible, antibacterial as well as antitoxic immunity by vaccination with vaccines incorporating not only the toxin or toxins but the streptococci. This possibility is suggested by the results of experiments in active immunization of rabbits, which, incidentally, tend to indicate also that the streptococci of scarlet fever possess specificity for the disease.

ORR, Buffalo.

PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **54**:413 (March 17) 1939.

For the period of Jan. 29 to Feb. 25, 1939, the incidence of smallpox, although only about 70 per cent of that at the same period last year, was still 75 per cent above the median. This increase appeared to be in the western and central parts of the United States. The incidence respectively of influenza, measles, poliomyelitis, diphtheria, typhoid, scarlet fever and meningitis was below median. The average mortality was 13.2 per thousand, which is above that of the corresponding period of last year, but below that of the corresponding periods in the two preceding years.

SANFORD, Chicago.

POLIOMYELITIS. M. FORRESTER-BROWN, Practitioner **142**:495 (April) 1939.

Forrester-Brown gives a short but comprehensive clinical discussion of this extensive subject.

GELSTON, San Francisco.

DIPHTHERITIC PARALYSIS AND ANTISTREPTOCOCCIC SERUM. P. MANGABEIRA-ALBERNAZ, Paris méd. **1**:418 (May 8) 1937.

Two patients with paralysis of the soft palate due to diphtheria made a rapid recovery following injections of antistreptococcus serum. One had received diphtheria antitoxin at the time of the acute infection, two months earlier. The other's disease was of the same duration, but this patient had received no antitoxin.

LESLIE, Evanston, Ill.

TREATMENT OF ACUTE ANTERIOR POLIOMYELITIS WITH THE CEREBROSPINAL FLUID FROM CONVALESCENTS. R. MEYER, Rev. franç. de pédiat. **14**:517, 1938.

In a small series of experiments, when cerebrospinal fluid from persons convalescing from poliomyelitis was mixed with the virus prior to inoculation of monkeys, it was effective in protecting them against infection. Thirteen patients with poliomyelitis were treated with cerebrospinal fluid from convalescents, with gratifying results, compared with those in patients not so treated. The final judgment of the results was deferred until eight months after the acute illness. On the day of diagnosis 20 to 30 cc. was given intravenously and 20 to 30 cc. intramuscularly. On two successive days the intramuscular injection was repeated. Meyer feels that cerebrospinal fluid is easier to obtain than serum, that it is as effective, if not more effective, than serum and that the removal of cerebrospinal fluid from the convalescent produces no harmful effects and may be beneficial to him.

LESLIE, Evanston, Ill.

CHICKENPOX AND HERPES ZOSTER. P. DURAND, Presse méd. **47**:212 (Feb. 8) 1939.

A 5 year old child during typical chickenpox presented lesions along the genital branch of the genitocrural nerve. The lesions disappeared exactly at the same time as the generalized eruption. A 60 year old man had typical herpes zoster of the left leg, accompanied by a generalized pustular rash. Pain was present only over the lesions on the leg. There was no fever, and no lesions of the mouth. Following this patient's recovery, chickenpox developed in a grandchild.

DAFFINEE, Boston.

CHOLESTEROL AND ASCORBIC ACID IN THE ADRENAL CAPSULE AS AFFECTED BY DIPHTHERIA TOXIN. G. CAREDDU and J. WILCZEK, Riv. di clin. pediat. **37**: 130 (Feb.) 1939.

The ascorbic acid content of the adrenal glands of young guinea pigs averaged 0.927 mg. per gram of the organ and that of adult guinea pigs 0.673 mg. When diphtheria toxin was given to guinea pigs, a diminution in the amount of ascorbic

acid resulted. The more intense the hemorrhage into the adrenals the greater this diminution became. In 1 animal receiving 2.5 minimal lethal doses of diphtheria toxin the ascorbic acid was only 0.067 mg. per gram of organ. The free cholesterol in the blood shows a marked reduction following the giving of diphtheria toxin. The cholesterol in the blood, both free and combined, diminished nearly proportionally to the dose of toxin given. HIGGINS, Boston.

ACUTE INFECTIOUS DISEASES IN EARLY INFANCY. H. ZISCHINSKY, Jahrb. f. Kinderh. **148**:113 (Dec.) 1936.

Scarlet fever was found occurring in several infants in the first few weeks of life. Breast feeding seemed to give no protection. A number of these very young patients were afebrile. The rash was similar to that in older children. The usual complications seen in older children were found. The prognosis of scarlet fever occurring in the first year of life is less favorable than that of scarlet fever in general but is more favorable than that of measles occurring so early.

Chickenpox was relatively infrequent in early infancy. There was a progressive increase in the period from the age of 1 to 12 months. The fatal cases were complicated by other conditions. For example, 9 cases in which the disease ended fatally were complicated by tuberculosis. Chickenpox in uncomplicated cases was generally mild. There were numerous cases in which pyoderma was present. The cases complicated with other infectious diseases were often serious. The exanthem in a child of 6 months was hemorrhagic in type.

In 3 infants erythema infectiosum was seen. In none was it serious. The characteristic rash was present.

Pharyngeal diphtheria in the very young was divided into mild, moderately severe and grave. The complications were similar to those in older groups. In addition to the usual cardiac disturbances and those due to polyneuritis, erysipelas and dysentery were found also.

Laryngeal, nasal, conjunctival, cutaneous and wound diphtheria were also reported.

A good many of the infants in whom diphtheria occurred in the first six months were breast fed.

The general mortality was 42.4 per cent for those in the first half year and 36.47 per cent for those in the second half year of life.

Mumps was not found to occur in the first year of life.

Pertussis was found in a large number of young infants. The incidence of pulmonary complications, septic complications, dysentery, diphtheria, varicella and measles was great. The prognosis of pertussis in this age group is distinctly unfavorable.

Dysentery was found in 40 infants in the first year of life, with a mortality of more than 50 per cent.

Three cases of mild typhoid were reported, all of which were complication free. The infants all recovered.

Epidemic meningitis was found in a 2 month old breast-fed child. The findings of meningeal involvement were typical. The child died shortly after hospitalization.

LANDAU, Hannibal, Mo.

PERMANENT IMPAIRMENT OF THE HEART AFTER DIPHTHERIA. A. BEER, Jahrb. f. Kinderh. **148**:152 (Dec.) 1936.

The literature concerning the duration of diphtheritic cardiac changes is considered. Anderson is quoted as saying that symptoms of such changes may appear at the age of 50 or 60 years, when the degenerative diseases set in. Numerous cases have been reported which lend credence to the idea that diphtheritic changes last for years. The author concludes, however, that more careful consideration and study must be given to this problem before it is solved.

LANDAU, Hannibal, Mo.

DIPHTHERIA. O. ROSTOSKI, München. med. Wchnschr. **85**:434 (March 25) 1938.

In this lecture on diphtheria Rostoski gives many interesting personal observations. Since 1930 there has been a marked increase in the incidence of diphtheria in Germany. The peak was reached in 1936 (according to the last available statistics when the lecture was given). The following table gives the numbers of cases reported since 1925:

1925	36,296	1931	56,628
1926	30,302	1932	64,138
1927	33,542	1933	74,558
1928	41,160	1934	113,936
1929	49,023	1935	132,930
1930	70,855	1936	149,973

Not only are there more cases, but there is an increase in those of the type of diphtheria which one designates as malignant, toxic or septic. In most of the cases of the serious type the infection is caused by the intermedius or gravis form of the diphtheria bacillus. In order to be effective, antitoxin must be given earlier in these cases than in those of infection with the mitis form.

The author observed 1,217 cases in seven years. In 1 instance the incubation period was less than twenty-four hours. Relapses occurred in 4 of 340 cases in 1935 and in 7 of 464 cases in 1936. Two relapses occurred within two weeks of the original infection; the others, up to forty-seven days after the original infection. About half the patients had marked enlargement of the cervical lymph nodes, but most of these nodes subsided without suppuration. Cultures were taken from those requiring incision. The cultures were either sterile or showed diphtheria bacilli; they never showed streptococci. Cultures made in 30 cases of tonsillar abscess showed streptococci in only 1. Similarly cultures in many instances of suppurative otitis media were either sterile or showed diphtheria bacilli.

Rostoski observed paralysis as a complication in 101 patients. All of them recovered. Involvement of the larynx and bronchi was infrequent, and only 4 tracheotomies were necessary. Deaths resulted from circulatory failure, due primarily to toxic myocarditis.

Electrocardiographic changes are presented at length. There is an alteration in the electrocardiogram before macroscopic or microscopic changes occur in the heart muscle. Autopsies failed to reveal anatomic changes before the seventh or eighth day of illness in cases in which electrocardiographic tracings were abnormal. The prognosis in cases with myocardial injury is most important. There are wide differences of opinion on the subject. Most of the author's patients were clinically well, with normal electrocardiographic tracings, after three to five months. Although the follow-up observations are not complete, it seems that the prognosis is good.

Serum therapy has been criticized frequently in Germany during the past few years. Rostoski summarizes his results as follows: Serum was given on the first day of illness to 99 patients, and none died; on the second day to 445, with a death rate of 2.5 per cent; on the third day to 544, with a death rate of 2 per cent; on the fourth day to 316, with a death rate of 6.6 per cent. After the fifth day the death rate is not influenced by serotherapy. This reemphasizes the importance of early administration of serum without waiting for bacteriologic confirmation of the diagnosis. The dose is from 300 to 500 units per kilogram of body weight, depending on the severity of the disease. The reactions from intravenous administration are severe; therefore most of the serum should be given intramuscularly and perhaps a small amount intravenously.

BRAHDY, Mount Vernon, N. Y.

THE BLOOD-SPINAL FLUID BARRIER IN EXPERIMENTAL POLIOMYELITIS. M. KASAHARA, T. KAKUSUI and SHA-SHI-NAN, Ztschr. f. Kinderh. **60**:391 (Dec.) 1938.

The authors tested the clinical evidence of increased permeability of the leptomeninges in poliomyelitis by giving a fuchsin dye intravenously to normal monkeys and to monkeys with experimental poliomyelitis. They found considerable increase in permeability.

SIEMSEN, Chicago.

Acute Infectious Diseases

EFFECT OF VARIOUS DILUENTS ACTING FOR SHORT PERIODS ON RABIES VIRUS IN HIGH DILUTIONS. D. F. MILAN, Am. J. Trop. Med. **19**:297-303 (May) 1939.

Studies were made on dilutions of rabies virus varying from 1:10,000 to 1:10,000,000, with different diluents being used. Distilled water was slightly less harmful than hormone broth to the virus. Physiologic solution of sodium chloride was definitely harmful in one hour. When a 10 per cent normal serum was added to the diluent, the unfavorable effect of the latter on the virus was reduced. Serum–tyrode solution was found to be the least harmful of the diluents tested, but serum-water was the most practical on account of the ease of its preparation.

BURPEE, Augusta, Ga.

IMMUNIZATION AGAINST RABIES USING AVIRULENT PURIFIED VACCINES. C. A. BEHRENS, L. B. SCHWEIGER, J. F. BARKER and J. L. REEVES, J. Infect. Dis. **64**:252 (May-June) 1939.

Behrens and co-workers started out to prepare a rabies vaccine with as little foreign matter as possible. The technical methods need not be pursued. It is only necessary to cite their conclusion: Vaccines made from precipitates obtained from purified rabic emulsions are not satisfactory as immunizing agents.

TOOMEY, Cleveland.

JUVENILE RHEUMATISM. C. M. POUNDERS and J. K. GRAY, South. M. J. **32**:471 (May) 1939.

Pounders and Gray believe that juvenile rheumatism is a systemic disease of unknown cause, chronic and subject to repeated exacerbations. Its chief clinical manifestations result from invasion of the heart, the joints and periarticular structures, the nervous system and the subcutaneous tissues.

It is predominantly a disease of school age and flourishes among the poor, i. e., where there are overcrowding, bad sanitation, improper heating and damp dwellings.

It is of great importance because of its contribution to cardiac invalidism and death both during childhood and later adult life.

The treatment of active rheumatism consists in insuring long periods of rest, nourishing food and proper hygiene with gradual resumption of exercise after the activity of the infection is thought to be arrested.

SCHLUTZ, Chicago.

PNEUMOCOCCEMIA IN AN INFANT OF SEVEN DAYS TREATED WITH SULFANILAMIDE UNSUCCESSFULLY. J. DELON and R. GIRET, Arch. de méd. d. enf. **42**:380 (June) 1939.

A full term normal infant, born without incident, of healthy parents, remained well up to the seventh postnatal day. Then the temperature suddenly rose to 39 C. (102.2 F.); the baby became dyspneic; there was marked cyanosis with a dry cough. The respiratory rate was 50 per minute. A herpetic eruption appeared on the right cheek. Fine rales could be heard throughout the entire pulmonary area. A tentative diagnosis of acute pulmonary edema was made, and within the next twenty-four hours the baby received 20 cc. of antipneumococcus serum and

three injections of physiologic solution of sodium chloride containing a total of 40 centigrams of sulfanilamide. In addition, mustard baths were employed, and oxygen was administered for five minutes each hour. The nose and throat were treated with mild astringents. The following day the patient was visibly improved; the administration of sulfanilamide was continued in diminishing doses, so that within three days the baby had received 75 centigrams. The weight loss was 300 Gm. Four days later, diarrhea developed, with tympanites. Roentgenologic examination showed an area of consolidation near the right hilus. The baby was discharged in fair condition on the twelfth day and was followed in the outpatient division; after two weeks anorexia was noted; the tympanitic syndrome returned; there was marked constipation as well as hypertrophy of the liver and of the spleen. The temperature was normal. The enlargement of the liver and spleen continued, and, in addition, a discrete mass could be felt in each flank. Pneumococcic peritonitis was considered, but exploratory puncture was refused. Sulfanilamide solution was injected to the total amount of 75 centigrams, without effect.

Roentgenographic studies with a barium sulfate meal showed that the intestinal distention involved chiefly the transverse colon. Ascites was present. Surgical intervention having been refused, roentgen therapy was instituted, but after a single exposure the patient was removed to the service of Weill-Halle, who reported the onset of epistaxis, with numerous and rapidly spreading ecchymoses. Death followed in four days.

AMESSE, Denver.

GRAVE ATYPICAL TYPHOID FEVER COMPLICATED BY POLYNEURITIS. P. WEILL-HALLÉ, B. KLOTZ and F. LAUTMANN, Bull. Soc. pédiat. de Paris **36**:658 (Nov.) 1938.

A girl 12½ years old had severe typhoid fever. Bacillus typhosis was not cultured from the blood until the sixth week of illness, although a number of blood cultures were made previously. The agglutination test with the same organism was not positive until the ninth week. Bronchopneumonia and polyneuritis developed as complications. The patient recovered. A nurse who had been in contact with her contracted typhoid fever, although during twenty years in the hospital she had repeatedly attended patients with that disease without having contracted it.

BENJAMIN, Montreal, Canada.

ANTECEDENT MATERNAL RHEUMATISM WITH A FAMILIAL FORM OF BROUILLARD'S DISEASE AFFECTING THREE CHILDREN OF FOUR. G. BLECHMANN and L. MÉNARD, Rev. franç. de pédiat. **14**:292, 1938.

In a family of 4 children the 3 boys showed rheumatic manifestations, while the girl escaped the condition. The mother had had acute rheumatic fever at 18 years of age.

LESLIE, Evanston, Ill.

FURTHER OBSERVATIONS ON THE DEVELOPMENT OF HUMORAL ANTISTAPHYLOCOCCUS IMMUNITY FOLLOWING INJECTIONS OF SPECIFIC ANATOXIN. G. BROGI, Lattante **10**:193 (May) 1939.

In children intradermal injections of Ramon's staphylococcic anatoxin were more successful than subcutaneous injections in producing antitoxin in the blood. The routine method of three subcutaneous injections at five day intervals increased the antitoxic titer of the blood to between 4 and 15 units per cubic centimeter. Neither vitamin B nor vitamin C nor Haemophilus pertussis vaccine had any effect on the building up of staphylococcic antitoxin in the blood.

HIGGINS, Boston.

LEPTOSPIROSIS TYPHOSA. D. VON MORITZ and A. ILLENYI, Monatschr. f. Kinderh. **78**:193 (May) 1939.

Von Moritz and Illenyi report 6 cases of a disease with a sudden onset, other features of which were high fever, nausea, vomiting and abdominal pain. The duration was about seven days, the fever ending by lysis. In some cases there was a papular exanthem. The liver and spleen were palpable. The laboratory tests for typhoid and paratyphoid were negative. Because of a similar epidemic in the neighborhood, the writers suspected a spirochetal infection. To isolate the organism, they examined the sediment of thrice centrifuged citrated blood with the dark field; they inoculated mice with the sediment; they attempted to culture it on artificial mediums, and they determined the agglutinations. The results showed leptospirosis typhosa.

GERSTLEY, Chicago.

VALUE OF THE WIDAL AGGLUTINATION TEST IN THE DIAGNOSIS OF TYPHOID FEVER IN THE TROPICS. J. E. DINGER, Nederl. tijdschr. v. geneesk. **83**:10 (Jan. 7) 1939.

Dinger, working in Batavia, capital of Java and the Netherland East Indies, comes to the following conclusions. In regions where typhoid fever is endemic Widal's test qualitatively as well as quantitatively has only a relative diagnostic value, especially if in these regions vaccination against typhoid fever is done regularly. In nonendemic regions, for instance, Holland, where vaccination is not done regularly, an agglutination titer of even 1:100 has diagnostic significance.

VAN CREVELD, Amsterdam, Netherlands.

OTOGENIC TETANUS. J. VAN DER HOEDEN and F. L. J. JORDAN, Nederl. tijdschr. v. geneesk. **83**:2449 (May 27) 1939.

A man of 38 and a boy of 7 years had tetanus originating from a focus in the middle ear. The simultaneous presence of tetanus bacilli and aerobic microorganisms is considered as a factor promoting the development of the former infection. In cases of tetanus in which no source of entry can be detected, it is advisable to consider the possibility of an infection of the middle ear. In accordance with the observations of others, in both patients the progress was favorable, no surgical intervention being necessary.

VAN CREVELD, Amsterdam, Netherlands.

Chronic Infectious Diseases

CONGENITAL NEUROSYPHILIS—REPORT OF A CASE WITH UNUSUAL ENCEPHALOGRAPHIC CHANGES. G. M. WYATT and B. W. CAREY JR., Am. J. Roentgenol. **41**:779 (May) 1939.

A case of congenital neurosyphilis with syphilitic meningitis is reported. The patient, a white girl, was admitted to the hospital at the age of 10 weeks with many signs of syphilis, including a positive Hinton reaction of the blood, papular syphilids and generalized superficial lymphadenopathy. The roentgen appearance of the long bones was reported as diagnostic of congenital syphilis. The patient was given courses of antisyphilitic therapy. At the age of 6 months the Wassermann reaction of the spinal fluid and the Hinton reaction of the blood were still positive. The encephalogram showed dilated lateral and third ventricles and deep, wide cortical sulci. The gyri appeared small. At the age of 18 months the Hinton reaction of the blood was still positive and the colloidal gold curve was 0000000000, but the Wassermann reaction of the spinal fluid was negative. At this time there was still dilatation of the ventricles, but there was apparent marked increase in the amount of cortical tissue as compared with that observed in the encephalograms at 6 months.

SQUIRE, Chicago.

THE FATE OF CHILDREN WITH PRIMARY TUBERCULOSIS. PHILLIP T. Y. CH'IU, J. A. MYERS and C. A. STEWART, J. A. M. A. **112**:1306 (April 8) 1939.

The aim of this study was to evaluate the prognostic significance of a positive and a negative reaction to tuberculin. Only children who were followed for ten years or more were included. Of 446 children who had positive tuberculin reactions when first seen, there developed evidences of the reinfection type of tuberculosis in 67 (15 per cent). Of 772 with negative reactions at the outset only 13 (1.7 per cent) had the disease. Twenty-three of the 446 originally positive reactors died within the ten year period. The mortality in the group with positive reactions was 38 times that in the group with negative reactions.

HEERSMA, Kalamazoo, Mich.

END RESULT OF A TUBERCULOSIS CASE-FINDING PROJECT. J. B. NOVAK and J. S. KRUGLICK, J. A. M. A. **112**:1452 (April 15) 1939.

In routine testing of high school students for tuberculosis, 55 cases were discovered. In 45 the involvement was minimal, in 19 moderately advanced and in 1 far advanced. Follow-up three to five years later revealed the startling paradox of 6 deaths among the group with minimal involvement and only 1 in the group with advanced involvement. Eight of the group with incipient infection showed advanced processes. The authors feel that the seriousness of a positive reaction in an apparently healthy adolescent is not appreciated.

HEERSMA, Kalamazoo, Mich.

A TUBERCULOUS EPIDEMIC CAUSED BY MILK-BORNE INFECTION. SIMON STAHL, Brit. J. Child. Dis. **36**:83 (April-June) 1939.

In the end of August and the beginning of September 1936 several children fell ill with various tuberculous symptoms in the small community of Horred, Sweden. The infection was traced to a cow with recent tuberculosis of the udder in a herd of 22 cows. The cows had been examined as recently as May 1936 (there is no mention, however, of their having been tested with tuberculin). Fifty of 134 school children had consumed the infected milk; of these, 45 gave a positive reaction to tuberculin. Only 8 of those who had not consumed the infected milk gave a positive reaction. Several of the infected children were very ill. The disease manifested itself in the form of lymphoma of the hilus, erythema nodosum, cervical adenitis, mesenteric lymphadenitis and phlyctenular conjunctivitis.

The doctrine that tuberculous milk is a desirable means of immunization seems pretty well refuted. Any method capable of producing tuberculous meningitis is too dangerous to employ.

LANGMANN, New York.

CONGENITAL ATROPHY OF THE EXTERNAL EAR IN CASES OF HEREDOSYPHILIS. A. TOURAINE and L. GOLÉ, Bull. Soc. franç. de dermat. et syph. **46**:90 (Feb.) 1939.

The authors state that malformations of the ear in patients with congenital syphilis are not altogether exceptional and may vary from simple hypoplasia of the auricle to complete absence of the external, middle and internal ear. They cite the case of a 15 year old child with congenital syphilis, one of the presenting signs of which was atrophy of the left ear.

LAYMON, Minneapolis. [ARCH. DERMAT. & SYPH.]

VALUE OF THE PERCUTANEOUS REACTION: ITS IMPORTANCE IN THE DISCOVERY OF TUBERCULOSIS AMONG GROUPS OF CHILDREN. G. DREYFUSS-SÉE, Bull. Soc. pédiat. de Paris **36**:497 (July) 1938.

In percutaneous and cutaneous tests on 425 children, with the use of Pasteur Institute tuberculin, another tuberculin and an anatuberculin (which is a concen-

trated tuberculin treated with a solution of formaldehyde in wood alcohol and water), practically complete agreement was obtained in the numbers of positive and negative reactions. There was disagreement in the reactions to the Pasteur tuberculin in 5 out of the total of 425 children; these 5 gave positive reactions to cutaneous tests and negative ones to percutaneous tests. Intradermal tests with 1:100 tuberculin elicited positive reactions in all of the 5 children, and percutaneous tests which were repeated with anatuberculin also gave positive responses. Percutaneous tests can be read by persons with little experience and on the sixth to the eighth day after their performance. The simplicity of the technic of the test, performed as it is without the use of a needle, makes it readily acceptable to parents and children. It is recommended for use among large groups of children, as, for example, in schools.

BENJAMIN, Montreal, Canada.

PERCUTANEOUS TUBERCULIN REACTION. LESNÉ, RADENAC and M. LÉVY, Bull. Soc. pédiat. de Paris **36**:504 (July) 1938.

The tuberculin test performed by inunction is less sensitive than that by scarification but if concentrated tuberculin is employed for the former it is as effective as the ordinary tuberculin used in the latter. Eight hundred and fifty-five children from 2 to 14 years of age were tested cutaneously with Pasteur Institute tuberculin and percutaneously with concentrated tuberculin. Two hundred and forty-two gave positive reactions to both tests, 11 had positive percutaneous and negative cutaneous reactions; none had reactions which showed the reverse disagreement. Five of the 11 children in whom the results of the two tests showed discrepancy were again subjected to cutaneous tests, and 3 gave positive while 2 had negative responses again.

In the performance of the percutaneous test an area of skin of about 2 sq. cm. is rubbed with a gloved finger for half a minute, until redness appears; a drop of tuberculin is then placed on the reddened area of skin and rubbed in for half a minute. The result is observed after four to six days or later. When the reaction is positive, papules or papules and vesicles develop on a reddened base. The reaction disappears gradually and after eight to fifteen days imparts to the finger a grating sensation of tiny, finely indurated papules. It disappears entirely in three to five weeks. No infection, ulceration or scarring occurs.

BENJAMIN, Montreal, Canada.

SCHOOL MEDICINE AND TUBERCULOSIS. A. BOHN, Bull. Soc. pédiat. de Paris **36**:700 (Nov.) 1938.

Repeated tuberculin tests at regular intervals are advocated for school children. Fluoroscopic examinations of the chests of school children were made in order to detect abnormalities in those who were known to have positive tuberculin tests, and to show the need of testing with tuberculin of all those who had not been given the tuberculin test but in whose lungs suggestive shadows appeared. The school personnel were also fluoroscopically examined for tuberculosis. Bohn states emphatically that school, family and dispensary physicians as well as nurses from dispensaries and schools who visit in the homes, must all cooperate in a comprehensive program to detect tuberculosis in patients encountered both in and outside of schools.

BENJAMIN, Montreal, Canada.

IS THE PILONIDAL SINUS A SURE SIGN OF CONGENITAL SYPHILIS? ANDRÉ BELEY, Gaz. d. hôp. **112**:21 (Jan. 7) 1939.

The author examined 100 mentally retarded children who had some "suggestive" evidence of congenital syphilis, and found the pilonidal sinus present in 51 per cent. He divided the cases into two groups. Pilonidal sinus was present in 67 per cent of the children with "definite" evidence of congenital syphilis, such as history of

syphilis in the parents, neonatal signs, persistent hydrocele or a positive Wassermann reaction. It was present in only 41 per cent of the other group, in which the diagnosis of syphilis was less "convincing."

On this questionable evidence he claims that the presence of pilonidal sinus is an almost certain sign of congenital syphilis.

KAJDI, Baltimore.

ABSENCE OF CUTANEOUS ALLERGY TO TUBERCULIN IN TUBERCULOUS CHILDREN. G. PAISSEAU, J. VALTIS and F. VAN DEINSE, Presse méd. **47**:307 (Feb. 25) 1939.

Three cases of negative cutaneous reactions to tuberculin in definitely tuberculous children are presented. The authors state that because of the clinical form of the disease and the physical condition of the patients the phenomenon could not be explained on the basis of transient anergy or the prolongation of an antiallergic period.

DAFFINEE, Boston.

CHANGES IN THE CEREBROSPINAL FLUID OF INFANTS WITH CONGENITAL SYPHILIS. NELLA CLERICI, Med. ital. **20**:134 (March 31) 1939.

The chemistry of the normal cerebrospinal fluid is reviewed. Lumbar puncture was done on 32 children. Nineteen were under 2 years and 13 were over 2 years. Of those under 2 years, only 15 showed changes in the spinal fluid. Of those over 2 years, 6 showed changes in the fluid. The most frequent changes were an increase in the lymphocytes and an increase in the albumin. The value for sugar in the spinal fluid was normal in all cases. The Wassermann reaction was positive in 7 cases. Changes in the spinal fluid occurred in infants with cutaneous signs of syphilis and in those with symptoms referable to the nervous system.

MARTOCCIO, Utica, N. Y.

ENTEROGENOUS INFANTILE TUBERCULOSIS. FELICE MELLONI, Med. ital. **20**:198 (April 30) 1939.

The author reports a case of extensive tuberculous infection of the gastrointestinal tract of a 12 month old infant. The diagnosis was confirmed at autopsy. There was involvement of the intestine from the ileocecal valve to the last portion of the ileum. The ulcerated areas were the size of lentils, and the edges were undermined. The mesenteric lymph glands were considerably enlarged. From animal inoculation the authors conclude that the bovine bacilli were the cause of the lesion and that it was primary in the intestine. Autopsy did not reveal any pulmonary involvement. Such cases, according to the author, are rare.

MARTOCCIO, Utica, N. Y.

PROPHYLAXIS OF TUBERCULOUS INFECTION. R. VAGLIO, Med. ital. **20**:291 (June) 1939.

The author points out the various ways in which a child may become infected with the tubercle bacilli. The most important of these is intimate contact with infected older persons in the home. An important focus may be found in the school room, where the teacher may be infected. The portals of entry are the respiratory tract and the digestive tract. The manner in which the infection spreads from the lungs to the other parts of the body is described. The von Pirquet and Mantoux tests are described. A state of anergy may be produced by measles or pertussis, less frequently by influenza, pneumonia or disturbances of the liver and occasionally by typhoid, scarlet fever, rheumatism or syphilis.

The two periods in which one must be most careful in searching out tuberculosis are just before the fifth year and after the fifteenth.

Vaccination against tuberculosis according to the method of Calmette is discussed, as are also that of Maragliano and that of Petragnani. In spite of all these methods of vaccination the author concludes that the best procedure is to keep the child away from foci of infection.

MARTOCCIO, Utica, N. Y.

STATISTICAL, CLINICAL AND ANATOMIC CONTRIBUTIONS TO RECOGNITION OF TUBERCULOUS MENINGITIS IN INFANCY. F. PONTIERI, Med. ital. **20**:321 (July) 1939.

The author reviews 228 cases of tuberculous meningitis in infancy in Milan, Italy, from 1924 to 1938. Tuberculous meningitis was more frequent in the first two years of life. In the first year there were 47 cases, in the second year 42 cases, in the third year 26 cases, in the fourth year 19 cases and in the fifth year 21 cases. In the subsequent years there was a progressive diminution up to the twelfth year.

The greatest seasonal incidence was at the end of winter and in the spring. The etiology, pathogenesis and pathologic anatomy are discussed. There were 178 autopsies. Photomicrographs of the pathologic process in the brain are presented. In 144 cases the lungs were also involved, in three fifths both lungs and more often the right than the left one in the remaining cases. The symptoms and course of the disease are discussed. (To be continued.)

MARTOCCIO, Utica, N. Y.

STATISTICAL, CLINICAL AND ANATOMIC CONTRIBUTIONS TO RECOGNITION OF TUBERCULOUS MENINGITIS IN INFANCY (CONTINUED FROM JULY 1939). F. PONTIERI, Med. ital. **20**:373 (Aug.) 1939.

The author discusses the pathogenesis and morphology of the symptoms of tuberculous meningitis. Delirium appeared in 18 per cent of his cases. Strabismus appeared in 32 per cent and ptosis in 14 per cent. Facial paralysis was present in 8 per cent, and the muscles of deglutition and of the tongue were involved in 0.5 per cent. There were 5 cases of hemiplegia.

Hyperesthesia was the most frequent sensory disturbance. The hydrocephalic cry was present in 15 per cent of the cases, and the author believes that this is an exterior manifestation of hyperesthesia. Hyperesthesia and somnolence often coexist. Headache was present in 28 per cent of the older children. The reflexes were variable. The Babinski sign was present in 20 per cent. Loss of weight and vomiting were frequently present.

The diagnosis and treatment are discussed.

MARTOCCIO, Utica, N. Y.

BACTERICIDAL POWER AGAINST TUBERCLE BACILLI IN SERUM OF NORMAL ANIMALS AND OF ANIMALS VACCINATED WITH DEAD TUBERCLE BACILLI. G. C. ABBA, Riv. di clin. pediat. **37**:504 (June) 1939.

Observations were made on rabbits. Blood serum was obtained before and thirty to forty days after the animal had received an injection of dead tubercle bacilli. The serum was mixed with live tubercle bacilli; the number of colonies of tubercle bacilli which could be grown at the time of the mixing and after twenty-four and forty-eight hours was determined. No increased bactericidal potency could be established.

HIGGINS, Boston.

EPITUBERCULOSIS AND PULMONARY ATELECTASIS. A. SCROGGIE, J. BAUZA, G. LLODRA and A. GUZMAN, Rev. chilena de pediat. **10**:61 (Feb.) 1939.

The authors report 11 cases. In all of the cases in which clinical and roentgen evidence showed epituberculosis, the authors were able by bronchographic procedures to demonstrate a bronchial obstruction and atelectasis in the affected zone.

In cases in which the atelectasis had passed into a chronic stage owing to fibrosis there was corresponding displacement of adjacent organs and tissues, due to retraction.

SCHLUTZ, Chicago.

COLLAPSE THERAPY FOR PULMONARY TUBERCULOSIS OF INFANCY. O. M. RODRIQUEZ, Rev. chilena de pediat. **10**:428 (July) 1939.

Early isolation of the young tuberculous child and placement under good hygienic and dietetic management constitute one of the major measures in the cure of this disorder.

The author believes that pneumothorax is of limited value for the young child. For the older child it seemed effective in only about one third of the author's cases.

This was partly due to difficulties encountered in maintaining it properly. In the group of cases in which it could be maintained successfully it hastened the cure of the patient. Maintaining pneumothorax in an infant is much more difficult than in an adult.

Paralyzing the diaphragm is a good procedure in certain forms of infantile tuberculosis and is often well associated with pneumothorax.

Both procedures must be supported by proper hygienic dietetic measures to insure the best results.

SCHLUTZ, Chicago.

TUBERCULOSIS OF THE PARENTS: ITS DEMOGRAPHIC SIGNIFICANCE. F. TORELLI, Med. inf., Rome **10**:141 (May) 1939.

Statistics are presented in the cases of 500 children one or both of whose parents had had pulmonary tuberculosis. In 56 per cent of the cases the mother alone was infected, in 23 per cent the father alone and in 21 per cent both parents. Fecundity in these families as compared with the population at large was not diminished. In 14 per cent of the cases in which the mother was ill and in 11 per cent of those in which the father was ill there were stillbirths. Deaths during the first year of life occurred in 25 per cent of the children whose mothers had the disease, in 22 per cent of those whose fathers were ill and in 26 per cent of those both of whose parents had tuberculosis.

HIGGINS, Boston.

SEARCH FOR TUBERCLE BACILLUS IN GASTRIC CONTENTS OF NURSLINGS RESIDING IN CONTAMINATED SURROUNDINGS. AXENTE IANCU, O. COMSIA and A. MANU, Med. inf., Bucuresti **1**:217 (May-June) 1939.

In searching for tubercle bacilli in the gastric contents of 15 infants residing in contaminated surroundings, 13 of whom had a positive Mantoux reaction and 2 a negative reaction, the authors found 9 with tubercle bacilli, 1 "doubtful" and 5 (including those with negative reactions) with no tubercle bacilli. Therefore, tubercle bacilli were found in 76.82 per cent of the cases. The sedimentation rate was increased in all cases, even those in which the Mantoux reaction was negative. These facts point to relative specificity of this reaction.

FROM THE AUTHORS' SUMMARY.

A CASE OF CONGENITAL HEPATOSPLENOGANGLIONIC TUBERCULOSIS; LEFT PRIMARY PULMONARY COMPLEX; MILIARY TUBERCULOSIS. TITU GANÉ, C. VASILESCO and SUZANA PETRESCO, Med. inf., Bucuresti **1**:217 (May-June) 1939.

A case of congenital tuberculosis is reported and a general review of the literature presented.

FROM THE AUTHORS' SUMMARY.

MINERAL METABOLISM: ITS PROGNOSTIC AND THERAPEUTIC VALUE IN JUVENILE TUBERCULOSIS. SMARANDA RADU, Med. inf., Bucuresti **1**:277 (May-June) 1939.

The levels of calcium and phosphorus in the blood vary in close accord with the clinical course of tuberculosis. In light forms and those of medium severity, but especially in recent infections in which clinical signs are absent but reactions to tuberculin are positive, the amount of calcium in the blood is less. The hypocalcemia seems to be due to demineralization of the organism. The value for calcium returns to normal or even drops below normal in severe forms or in forms

in which there is a tendency to recover. The phosphorus in the blood is, as a general rule, less sensitive to tuberculosis than is calcium, and the value is relatively higher. The therapeutic measures indicated to establish equilibrium of calcium and phosphorus in the blood, especially in grave forms of tuberculosis, are as follows: prolonged and repeated injections of calcium, alkaline phosphates and citrates; irradiation with ultraviolet ray (influences phosphorus especially); chrysotherapy, and administration of cod liver oil. FROM THE AUTHOR'S SUMMARY.

Diseases of Blood, Heart and Blood Vessels and Spleen

ENLARGEMENT OF THE HEART IN INFANTS AND YOUNG CHILDREN. M. A. KUGEL, Am. Heart J. **17**:602 (May) 1939.

Kugel describes an enlargement of the heart with a definite clinical syndrome as observed in 8 infants and young children. The cause is unknown. The symptoms usually occur suddenly and consist in rapid respiration, dyspnea and cyanosis. A fatal outcome occurs usually within a few days. The morbid anatomic picture consists in dilatation and hypertrophy of the heart, together with foci of atrophy and degeneration of muscle fibers. Glycogen stains of the heart muscle were found normal.

The differential diagnosis of cardiac enlargement in infancy and early childhood is discussed.

GIBSON, Chicago.

COARCTATION OF THE AORTA WITH ASSOCIATED STENOSIS OF THE RIGHT SUBCLAVIAN ARTERY. W. S. LOVE JR. and J. H. HOLMS, Am. Heart J. **17**:628 (May) 1939.

Love and Holms describe a case of coarctation of the aorta in which the unusual finding of a much lower blood pressure in the right arm than in the left was present. An adequate explanation of this clinical observation was seen in an associated stenosis of the right subclavian artery. So far as the authors have been able to ascertain, this is the first report of a case of this type to appear in the literature.

GIBSON, Chicago.

AN ELECTROCARDIOGRAPHIC STUDY OF TWINS. N. B. WISE, W. J. COMEAU and P. D. WHITE, Am. Heart J. **17**:701 (June) 1939.

An electrocardiographic study was made of 32 pairs of identical twins and 18 pairs of nonidentical twins. Varying degrees of similarity or difference have been found in the electrocardiograms of all the twins studied. Close similarity or no similarity may be found in the electrocardiograms of both identical and nonidentical twins, for which reason the identity or nonidentity of a given pair of twins cannot be determined from a study of their electrocardiograms alone, although identical twins did show a higher percentage of similar electrocardiograms than did nonidentical twins (a ratio of 16 to 32, compared with one of 4 to 18). The lack of absolute correspondence of the electrocardiograms of identical twins of the same height and weight emphasizes the individuality of the electrocardiogram.

GIBSON, Chicago.

ACUTE HEMOLYTIC (LEDERER'S?) ANEMIA. H. MCGAVACK, New England J. Med. **220**:140 (Jan. 26) 1939.

Hemolytic anemia in a girl of 17 years is reported which in its onset and early behavior simulated that described by Lederer and in its later course suggested Marchiafava's disease (Marchiafava, E.: Hemolytic Anemia with Permanent Hemosiderinuria, *Policlinico* [*sez. med.*] **38**:105, 1931; abstracted, *J. A. M. A.* **96**:2002 [June 6] 1931), but which throughout failed to satisfy all the usual criteria for either.

The disease resembled acute hemolytic anemia of the Lederer type in the following regards: the family history negative for blood dyscrasias; the sudden onset; the rapid development of severe anemia without demonstrable cause; the evidence of hemolysis as shown by the coloration of the skin; the positive van den Bergh reaction and hemoglobinuria, demonstrated on one occasion; the macrocytic type of blood response with high reticulocytosis, and the presence of many normoblasts and a few megaloblasts in the circulating blood; and the further indication of very active erythropoiesis as shown by a biopsy of bone marrow and a study of bone marrow blood.

The condition differed from Lederer's anemia in the following respects: the failure of the patient to respond to repeated transfusions; the presence of leukopenia and thrombopenia; the recurrent episodes of jaundice following splenectomy; the continuation of mild anemia and low grade fever for more than one year following the acute attack.

GENGENBACH, Denver.

CONCENTRATION OF PROTHROMBIN IN BLOOD OF BABIES. A. J. QUICK and A. M. GROSSMAN, Proc. Soc. Exper. Biol. & Med. **40**:647 (April) 1939.

A study of the blood of 8 infants from 3 to 7 days of age revealed that the prothrombin concentration as determined by the method of Quick (Nature of Bleeding in Jaundice, J. A. M. A. **110**:1658 [May 14] 1938) was essentially the same as that of the blood of normal adults.

HANSEN, Minneapolis.

STERNAL PUNCTURE IN THE DIAGNOSIS OF DISEASES OF THE BLOOD FORMING ORGANS. R. B. SCOTT, Quart. J. Med. **8**:127 (April) 1939.

This article describes the technic of sternal puncture and practical applications of it to normal and to diseased subjects. A very extensive bibliography and three plates, one in color, accompany the report.

BRADFORD, Rochester, N. Y.

ANEMIAS OF THE NEWBORN AND EARLY INFANCY. J. L. HENDERSON, Tr. Obst. Soc. Edinburgh, 1939, p. 49; in Edinburgh M. J., March 1939.

Henderson finds etiologically that there are six general types of anemia in the early months of life. Anemia of the premature has one phase in the first three or four months which is simply an exaggeration of the physiologic hemolysis of early infancy, characterized by hyperchromia. The second phase, which begins about the sixth month, is caused by a deficiency of iron and is attended by hypochromia. Hemorrhages are responsible for another group. Erythroblastosis includes three conditions: hemolytic anemia of the newborn, hydrops foetalis and icterus gravis. These three are of chief interest to the author, who reports cases and reproduces blood pictures and photomicrographs of the liver and kidney. Blood charts are presented of 3 infants with icterus gravis. The sixth type includes anemia due to infection, most commonly syphilis, and anemia due to a congenital deficiency of iron in the offspring of a mother who suffered from hypochromic anemia during the reproductive period.

NEFF, Kansas City, Mo.

ACTION OF LEUCOPOIETIC DRUGS. C. R. DAS GUPTA, Indian J. M. Research **26**: 947 (April 4) 1939.

Das Gupta, using rabbits, determined the effect of leukopoietic drugs on circulating leukocytes. Transient leukocytosis was brought about by pentnucleotide, sodium nucleinate, liver extract, histamine, epinephrine and acetylcholine. It was due partly to mobilization of leukocytes. There was no evidence that pentnucleotide or liver extract could accelerate the formation of white cells in health. Colchicine stimulates the proliferation of cells in the marrow, but the toxic effects outweigh the stimulating effect.

SNELLING, Toronto, Canada.

ESSENTIAL HYPERTENSION IN THE CHILD. J. GADRAT and W. FOURNIER, Arch. de méd. d. enf. **42**:257 (May) 1939.

In the category of arterial hypertension without chronic nephritis there is a type known as essential hypertension, wherein the deviation from the normal seems to constitute an entity. In time, however, renal disturbances are noted, at first intermittent, but finally assuming a permanent character, which persists to the end.

Certain English and American authors have suggested that a syndrome of malignant hypertension should be individualized, while French clinicians hold such a view still open to question.

An exhaustive clinical record is offered bearing on arterial hypertension in a boy of 11 without previous renal involvement, which terminated fatally in two months.

AMESSE, Denver.

PURPURA FULMINANS OF MENINGOCOCCIC ORIGIN TREATED BY SULFANILAMIDE WITH RECOVERY. L. RIBADEAU-DUMAS, J. CHABRUN and M. DUFOUR, Arch. de méd. d. enf. **42**:360 (June) 1939.

The advantages of the joint exhibition of chemotherapy and serotherapy in meningococcic diseases are well illustrated in a case reported by these authors. A 9 month old boy was admitted to a hospital on the fifth day of illness. There was a history of fever, angina and a severe convulsion. Examination showed a purpuric rash over the entire body; there were visceral hemorrhages, as expressed by hematemesis and melena, and bronchopneumonia was developing at the base of the left lung. Signs of meningeal irritation, however, were absent, although spinal puncture disclosed a distinctly purulent fluid containing many meningococci. Serum was given intraspinally and intramuscularly, and 1 Gm. of sulfanilamide, by mouth. The following day the clinical picture was not changed materially, but meningococci were absent from the spinal fluid. The injection of serum was repeated, using, in addition to the aforementioned routes, the intraventricular; the dosage of sulfanilamide was likewise repeated. This routine was carried out during the next three days. The baby reacted rather slowly; he showed vomiting, intestinal indigestion, rigidity of the neck, muscular twitching and trembling, while the temperature slowly subsided. From the eighth to the eighteenth day the amelioration was fairly rapid, but the administration of sulfanilamide was continued, 0.5 to 1 Gm. being given daily. The patient was discharged, completely recovered, on the twenty-first day.

Two further observations on infants are recorded. One recovered, and the other died.

AMESSE, Denver.

ASPIRATION OF BONE MARROW IN THE INFANT. M. LAMY, G. SÉE, P. CHICHE and C. MONTEFIORE, Nourrisson **27**:79 (March) 1939.

The ossification of the sternum is slow and permits aspiration of bone marrow, with any degree of certainty, only in children over 8 years of age. Up to that age the islands of bone tissue in the sternum are too small to be hit regularly. The authors consequently advise aspiration from the epiphysial region of the tibia. They puncture the tibia 2 to 3 cm. below the line of articulation of the knee joint and insert the needle 1 to 1.5 cm. in the bone. The red bone marrow of that region is replaced by yellow bone marrow at about the age of 8 years. In adults the authors found that the marrow contained 10 to 20 per cent erythroblasts per hundred nucleated cells and 60 per cent granulocytes. In newborn infants they found the number of erythroblasts increased to 45 to 50 per cent; there were also increased numbers of granulated elements. Lymphoid cells start to increase after the first week of life.

HEYMANN, Cleveland.

KAUFFMANN WATER DIURESIS TEST OF HEART FUNCTION IN CHILDREN. U. GRUNINGER and W. TUSSING, Jahrb. f. Kinderh. **148**:205 (Jan.) 1937.

This test was shown to be inaccurate in determining the presence of latent edema. Of 43 children with cardiac or circulatory disturbances, the test was inaccurate in 15.

This test can hardly be looked on as dependable since there are too many other factors that play a part, such as a labile character of the vasomotor nervous system, menstruation and obesity.

LANDAU, Hannibal, Mo.

FIBROMA OF THE HEART. A. SYMEONIDIS and A. J. LINZBACH, Virchows Arch. f. path. Anat. **302**:383, 1938.

From the literature relating to so-called fibroma of the heart, a term which usually refers to an organized thrombus, the authors select 6 cases that have distinguishing characteristics. To these they add 3 of their own. One of the patients was a newborn infant, the second a child of 15 months and the third a 53 year old man. The tumors of this special group were congenital and solitary; each was situated in the myocardium and increased slowly in size with growth of the heart. They were not encapsulated. They were composed of fibrous and elastic tissue, the latter increasing progressively with the age of the lesion, a fact which is interpreted as evidence of adaptation to cardiac function. They were neither inflammatory nor neoplastic but were congenital maldevelopments. A lesion of the type described is termed a fibroelastic hamartia. It is a maldevelopment of the interstitial tissue of the myocardium in the same way that the cardiac rhabdomyoma is a maldevelopment of the muscle.

SCHULTZ, Chicago. [ARCH. PATH.]

AURICULAR FLUTTER IN A CHILD. T. HALBERTSMA and H. A. P. HARTOG, Maandschr. v. kindergeneesk. **8**:213 (March) 1939.

In a girl of 2 years auricular flutter persisted during three years. The flutter disappeared and the sinus rhythm returned after administration of relatively high doses of digitalis; then, also, the symptoms of cardiac insufficiency disappeared. The child probably has an open foramen ovale. This is the fourth case described in the literature, and the second one in which the condition of the patient became normal after digitalis therapy. (Compare Amberg, S., and Willius, F. A.: Auricular Flutter with Congenital Heart Disease, Am. J. Dis. Child. **32**:99 [July] 1926.)

VAN CREVELD, Amsterdam, Netherlands.

A CASE OF APLASTIC ANEMIA. J. C. GUNST, Maandschr. v. kindergeneesk. **8**:320 (May) 1939.

Aplastic anemia was present in a boy 9 years old. A toxin as the cause of the disease could be excluded. The results of the autopsy were in favor of the diagnosis; a particular finding was a rather large quantity of hemosiderin in the liver. There is a discussion of the difficulties in the differential diagnosis.

VAN CREVELD, Amsterdam, Netherlands.

PURPURA AND THROMBOPENIA. W. A. BOEKELMAN, Nederl. tijdschr. v. geneesk. **83**:1325 (March 25) 1939.

Boekelman uses vital staining to determine the number of blood platelets. He gives the results obtained for 3 patients (2 adults and a boy of 3½ years) with severe hemorrhages of different kinds and petechiae. In the adults extirpation of the enlarged spleen was performed. This operation had a favorable effect on the patients, but only a temporary effect on the number of thrombocytes. Even after complete recovery the number of thrombocytes was still much too small.

So the thrombopenia cannot be the sole cause of the hemorrhages, but the spleen in some way or other has a large influence. There is an extensive discussion of different factors which play a role in purpura.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Nose, Throat and Ear

SOME SCHOOL HEARING SURVEYS: ANALYSIS AND OBSERVATIONS. E. M. FREUND New York State J. Med. **39**:1770 (Sept. 15) 1939.

A New York State law requires audiometric tests of all school children. Proper appliances and supervisors to carry out this law are provided. In 13,000 children 617 hearing defects have been found. Treatment, such as removal of tonsils and adenoids and attention to involved sinuses, should be carried out early if deafness is to be prevented. All children under 6 years of age found to have defects must be reported to the local health or welfare officer.

AIKMAN, Rochester, N. Y.

EVALUATION OF SULFANILAMIDE THERAPY IN ACUTE OTITIS MEDIA AND MASTOIDITIS. J. C. SCAL, New York State J. Med. **39**:1790 (Sept. 15) 1939.

Scal believes that sulfanilamide is contraindicated in the early stages of an ear infection. In acute mastoiditis, with sulfanilamide therapy the temperature may drop and all symptoms and tenderness disappear while roentgen examination still shows increasing destruction.

AIKMAN, Rochester, N. Y.

IMPORTANT FACTORS IN THE CONSERVATION OF HEARING. H. B. HITZ, Wisconsin M. J. **38**:382 (May) 1939.

One type of progressive hearing defect, beginning usually in the late teens, is variously diagnosed as chronic dry catarrh of the middle ear, hypertrophic and atrophic catarrh of the middle ear and by some, erroneously, otosclerosis. Its characteristics are diminished air conduction and increased bone conduction of sound and observable bulging or retraction of the tympanic membrane. Various causes, such as hereditary diseases, diseases of early childhood, social diseases, malnutrition and endocrine disturbances, as well as deficiencies of blood and growth, all have their advocates and critics.

Hitz believes that a large and decisive element in the causation of this progressive diminution in hearing is the fixed and chronic habit that some persons have of violently blowing the nose, causing excessive alternate inflation and deflation of the middle ear. Usually some transitory obstructive lesion initiates the habit, which then continues. Many writers have mentioned this factor of habitual pneumatic abuse. The cumulative effect of this increasing of air pressure incessantly repeated causes permanent changes in these delicate structures. Nature throws in more building material to strengthen against the physical strain; hence the impairment of hearing. Such effects of changing atmospheric pressure are had in an intensified way in airplane travel and cause a condition mentioned as "aero-otitis media acuta."

Treatment is chiefly preventive and consists in teaching children not to blow the nose forcefully. Both nostrils should be free when clearing the nose. Active treatment consists in breaking the habit and, on occasion, performing a minor surgical operation to increase ventilation.

The chronic snorer, continuously deflating his ears, is also often afflicted with regression of hearing. A correction of the nasal insufficiency improves this condition in some, and sleeping on the side rather than on the back leads to improvement in others.

JANNEY, Wauwatosa, Wis.

ROENTGEN THERAPY OF ADENOIDITIS. R. CLÉMENT, P. GIBERT and E. CLÉNET, Bull. Soc. pédiat. de Paris **36**:473 (July) 1938.

On very young children and on older ones on whom operation is not advisable, for example, children with persistent nasopharyngeal infection, chronic purpura, hemophilia, tuberculosis and recurrence of adenoiditis after repeated operation, roentgen therapy of adenoids was employed. Good results were observed sometimes after the first treatment but more commonly during the second week of therapy, after the third or the fourth treatment.

BENJAMIN, Montreal, Canada.

ACUTE LARYNGOTRACHEOBRONCHITIS. P. ROHMER, C. OBERLING and R. TULASNE, Rev. franç. de pédiat. **14**:283, 1938.

Two cases of laryngotracheobronchitis are reported. One of the patients was a child of 6 years and the other an infant of 11 months. In both the condition progressed rapidly to asphyxia and death. In neither was bronchoscopic aspiration used. The postmortem observations were characteristic: The bronchi were edematous and filled with thick tenacious material. Streptococcus haemolyticus and Friedländer's bacillus were found.

LESLIE, Evanston, Ill.

BEHAVIOR OF THE WHITE BLOOD CELLS AFTER TONSILLECTOMY. G. PELLICCIA, Arch. ital. di otol. **51**:84 (Feb.) 1939.

Recently Pelliccia studied the effect on the blood picture of massage of the tonsils. The most important finding was leukopenia. He next undertook an investigation of the effect of tonsillectomy on the blood of 15 patients, in 10 of whom massage of the tonsils had been carried out before the operation. As controls he used 5 patients who had had other operations comparable in gravity to tonsillectomy. In 3 of the controls appendectomy had been done. He discovered marked leukocytosis with an increase of neutrophils in the tonsillectomized patients, reaching its maximum five to seven hours after the operation, with return of the preoperative value after twenty-four hours. The variation in the number of lymphocytes was in inverse ratio to the variation in the number of neutrophils. Operative trauma or toxicoinfective factors played a small part in causing the changes in the blood, which are attributed to the sudden suppression of an action, perhaps endocrine, of the tonsils. This action, however, is shared by other aggregations of lymphoid tissue. The same effect was produced on the patients in whom the appendix was removed, but not on the other controls. The postoperative leukocytosis in cases of tonsillectomy was of brief duration because of the vicarious action of other lymphatic organs.

DENNIS, San Diego, Calif. [ARCH. OTOLARYNG.]

ASPIRATION OF A TOY IN CHILDHOOD. H. LÖFFLER, München. med. Wchnschr. **86**:260 (Feb. 17) 1939.

Löffler reports the case of a 13 month old infant who aspirated a toy nipple, 2 cc. in length. The infant cried out and collapsed and was immediately rushed to the hospital but was dead on arrival. Autopsy revealed the nipple obstructing the larynx. The nipple was the kind attached to toy nursing bottles for dolls. Löffler reemphasizes the danger of permitting little children who put things in their mouths to play with small toys.

BRAHDY, Mount Vernon, N. Y.

THE TONSILLAR COCCI AND THEIR SIGNIFICANCE. O. FELSENFELD, Bratisl. lek. listy **17**:203 (May) 1937.

After an intensive study of tonsillar cultures for two and a half years, the author summarizes the results as follows: Of the children in the vicinity of streptococcic infection, 50 per cent have tonsillar cultures positive for the hemolytic streptococcus, while only 20 per cent of average children have positive cultures. Seventy-five per cent of children with scarlet fever have positive cultures.

Children with mumps and chickenpox often have cultures positive for this streptococcus. In some cases of tonsillitis the percentage of positive cultures increases during convalescence. In most cases of scarlet fever the cultures become negative for the hemolytic streptococcus in four to five weeks. There is no relation to desquamation; some children had positive cultures when there was no sign of desquamation during the disease. Streptococcus viridans, enterococci and pleomorphic streptococci were observed to be about equally distributed, except that in mumps the percentage of Str. viridans was higher. Staphylococcus albus was observed especially in the tonsillar cultures of children with surgico-orthopedic tuberculosis, osteomyelitis and chickenpox. Staphylococcus aureus and Micrococcus tetragenus were observed to be equally distributed in all the cases examined. Since it is impractical to isolate a "coccus carrier," the prophylaxis against nasopharyngeal infection is accomplished by isolating the sick children, by using a disinfectant in washing both the patients and their utensils and by prophylactic inoculations.

STULIK, Chicago.

FAMILIAL HEREDITARY EPISTAXIS. C. G. VERVLOET, Nederl. tijdschr. v. geneesk. **83**:2232 (May 13) 1939.

Vervloet gives a description of several patients in two families with familial and hereditary epistaxis, thrombopenia and neutropenia. Liver treatment causes the epistaxis to disappear without changing the blood picture.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Lungs, Pleura and Mediastinum

BENIGN BRONCHOPULMONARY INFLAMMATIONS ASSOCIATED WITH TRANSIENT RADIOGRAPHIC SHADOWS. H. RAMSAY and J. G. SCADDING, Quart. J. Med. **8**:79 (April) 1939.

In the records of the tuberculosis dispensary in Walthamstow, England, the authors found 29 cases, in a group of 1,220 new cases, in which transitory roentgenologic opacities in the lung fields occurred without the symptoms which are usually found with pneumonic lesions. These cases were classified as follows: 4 of delayed resolution of acute pneumonia; 4 of lobar atelectasis and 21 which did not fall into either group. Ramsay and Scadding concluded that these localized consolidations probably represented aspiration pneumonia arising in the course of catarrhal infections of the respiratory tract.

BRADFORD, Rochester, N. Y.

ALVEOLAR AND BRONCHOPNEUMONIA IN CHILDHOOD. C. MCNEIL, Edinburgh M. J. **46**:153 (March) 1939.

McNeil gave this Honyman Gillespie Lecture on Aug. 25, 1938. He began with the statement that essentially any type of pneumonia is characterized by the presence of an inflammatory exudation into the alveolar spaces of the lungs, causing consolidation. Ten years ago McNeil brought out the term "alveolar pneumonia" to replace the commonly used term "lobar pneumonia," because it is a more accurate representation of the pathologic changes present. The inflammatory fibrinous exudate fills the alveolar spaces and their corresponding small bronchi, not extending to the walls of the alveoli, the walls of the bronchi or the interstitial stroma of the lungs. The micro-organism is the pneumococcus.

Bronchopneumonia is not so simple and is usually bilateral. The inflammation begins in the small bronchi, penetrates the epithelial and muscular layers and proceeds to the interstitial tissues and the adjoining alveolar spaces. Septicemia in a small number of cases is the source of bronchopneumonia; the infection comes from the blood stream to the lungs and produces inflammation in scattered foci, which develops into bronchopneumonia. The initial bronchitis may be due to the virus of measles, the bacillus of whooping cough, the influenza bacillus, a strepto-

coccus or a staphylococcus, but as it extends the pneumococcus may play a secondary and important role, with a fibrous exudate in the peripheral zones of consolidation. This illustrates the more complex pathologic and bacteriologic character of the bronchial type.

McNeil's conclusions are based on two series of cases, amounting in all to 1,013 cases. There are more cases of pneumonia of all types in the group aged from 1 month to 2 years than in that aged from 2 to 5 years or 5 to 12 years. The death rate in the group aged up to 2 years is three times as high as in the combined groups of ages from 2 to 12 years.

A clinical feature of importance is the sudden onset of uncomplicated alveolar pneumonia with delay in physical signs of disease in the lung.

NEFF, Kansas City, Mo.

CHYLOUS PLEURISY. S. GRACOSKI, E. HURMUZACHE and TITUS MĂRCULESCU, Bull. Soc. de pédiat. de Iasi **7**:35 (Jan.-June) 1937.

This rare condition is reported in a girl 3 years of age. The diagnosis was made from the character of the fluid obtained on thoracentesis. The child died. As autopsy was not permitted, the manner in which the condition developed was not discovered.

LESLIE, Evanston, Ill.

EMPYEMA IN AN INFANT THIRTEEN DAYS OLD. NAGEOTTE-WILBOUCHEWITCH, Bull. Soc. pédiat. de Paris **36**:726 (Nov.) 1938.

An infant on whom a rib resection for empyema of the right side of the chest had been performed in 1907 when she was 3 months old had at the time of this report become a woman, the mother of a family, and weighed 84 Kg.

BENJAMIN, Montreal, Canada.

PNEUMOTHORAX FOR PULMONARY ABSCESS. K. KOLLMEIER, München. med. Wchnschr. **85**:179 (Feb. 4) 1938.

Pneumothorax for pulmonary abscess may result in involvement of the pleura or in empyema. Kollmeier used pneumothorax in 7 of 10 cases of pulmonary abscess. In all but 1 case the abscess was either centrally located or near the hilus. Proper selection of cases, according to location of the abscess, is important. In none of the cases did pleural involvement develop. Only small quantities of air should be introduced, and refilling should be continued until the fever subsides and the cough and expectoration disappear. After the pneumothorax there was always general improvement, with decrease of fever, increase of appetite and decrease or cessation of the cough and expectoration. In the treatment of juxtapleural abscesses pneumothorax should be used with great caution or not at all.

BRAHDY, Mount Vernon, N. Y.

NONSYPHILITIC INTERSTITIAL PNEUMONIA OF INFANTS. O. AMMICH, Virchows Arch. f. path. Anat. **302**:539, 1938.

Ammich reports a study of interstitial pneumonia as observed in 14 infants in whom syphilis was excluded as a factor. Histologically and clinically the nonsyphilitic form of interstitial pneumonia is not to be distinguished from syphilitic pneumonia alba. The condition was observed chiefly in premature infants who lived from 1 day to 2½ months. The pulmonary lesion is considered a reaction of immature tissues to a variety of nonspecific noxa. Ammich holds that the pneumonia seen in syphilitic infants is not necessarily the result solely of the action of the infecting agent but may be the expression also of the reaction of an immature human organism. The 3 full term infants of the series, who lived four to eleven months, were examples of hypoplastic constitution; in these infants, also, immaturity of the tissue was held to be the essential factor.

SCHULTZ, Chicago. [ARCH. PATH.]

TREATMENT OF PNEUMONIA AND OTHER PNEUMOCOCCIC INFECTIONS BY MEANS OF SULFAPYRIDINE. L. A. HULST and F. L. J. JORDAN, Nederl. tijdschr. v. geneesk. **83**:1592 (April 8) 1939.

Figures are given referring to the lethality of lobar pneumonia in the University Hospital for Internal Diseases in Utrecht in the period from 1919 to 1937. A brief review is given of the literature on sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine), the special merits of which have been related particularly in regard to pneumococcic infections. The results obtained with this drug in 11 patients with pneumonia are recorded. The rapid fall of temperature was conspicuous, and in 2 patients pneumococci disappeared from the blood. A solely antipyretic action is improbable in view of experimental evidence and in view of the disappearance of pneumococci from the blood and cerebrospinal fluid.

One patient of this series died. The drug was found inactive or rather unsatisfactorily active in 2 patients. One patient with meningitis recovered, after having been treated without success with antimeningococcus serum and sulfanilamide. A further patient with pneumococcic meningitis recovered after combined treatment with specific serum, sulfanilamide and sulfapyridine (dagénan).

VAN CREVELD, Amsterdam, Netherlands.

SULFAPYRIDINE (DAGÉNAN) IN PNEUMONIA, BRONCHOPNEUMONIA, SEVERE INFLUENZA AND OTHER INFECTIONS. F. E. REVERS, Nederl. tijdschr. v. geneesk. **83**:1950 (April 29) 1939.

In several cases each, pneumonia, bronchopneumonia, purulent bronchitis and influenza have been treated with sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) with excellent results. The drug was administered in relatively high quantities during one to three days. VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

OCCURRENCE OF MONILIA IN NORMAL STOOLS. T. G. SCHOONER, Am. J. Trop. Med. **19**:163 (March) 1939.

Schooner studied the stools of a series of 314 normal persons by making cultures to determine the frequency of fungi in their gastrointestinal tracts. Monilia was found in 33.1 per cent of the stools cultured. As to types, Monilia albicans occurred in 16.9 per cent, Monilia parapsilosis in 6.0 per cent, Monilia krusei in 5.7 per cent and Monilia candida in 4 per cent. Other fungi isolated and identified were: Cryptococcus, in 28 per cent; Geotrichum, in 29 per cent; Penicillium, in 11.8 per cent, and Aspergillus, in 3.5 per cent.

BURPEE, Augusta, Ga.

ATRESIA ANI URETHRALIS. L. A. THUNIG, Arch. Surg. **38**:501 (March) 1939.

A rare anomaly is presented in which no anus was present, but a fistula extended between the urethra and the rectum. The patient, a boy, was operated on at forty-eight hours of age. An anus was made which was effective, with sphincteric control, for the period of eleven years during which the patient was under observation. The fistula between the rectum and the urethra was eradicated. A comprehensive account of the embryologic development of this anomaly is given.

KAISER, Rochester, N. Y.

CONTROL OF THE DISORDERED METABOLISM IN HYPERTROPHIC PYLORIC STENOSIS OF INFANCY. H. WILLIAMS, M. J. Australia **1**:414 (March 18) 1939.

Williams' studies show that the administration of saline solution in amounts of 750 to 1,500 cc. by the continuous intravenous drip method is much superior to

single small injections of saline solution in combating the dehydration, alkalosis and disordered chloride metabolism frequently associated with hypertrophic pyloric stenosis. As a result of such treatment the operative risk for the infant is lessened, and a better postoperative course is assured.

GONCE, Madison, Wis.

HYPERTROPHIC PYLORIC STENOSIS; OPERATION IN SPITE OF LYMPHADENITIS AND FEVER: CASE OF AN INFANT VACCINATED AT BIRTH WITH BCG, OPERATED ON AT AGE OF TWO MONTHS AND HAVING CERVICAL ADENITIS AND A POSITIVE CUTANEOUS REACTION TO TUBERCULIN TEST AT THREE YEARS. JEANNIN and DE GIRARDIER, Bull. Soc. pédiat. de Paris **36**:727 (Dec.) 1938.

A male infant 2 months old was operated on for pyloric stenosis. He had fever for fifteen days and generalized adenitis became more pronounced. His tuberculin test was negative at the time of operation and again one month later. When he was 3 years old, cervical adenitis developed on the right side of the neck. The tuberculin test had become positive. A roentgenogram of the chest showed no abnormality. This child had received BCG in the neonatal period. Lymphadenitis due to BCG may occur, and it is thought that the marked lymphadenopathy in this instance may have been due to the poor nutrition which was caused by excessive vomiting consequent to pyloric stenosis.

BENJAMIN, Montreal, Canada.

GLYCOGEN STORAGE DISEASE. F. GOLDMANN, Rev. franç. de pédiat. **14**:494, 1938.

Three cases of glycogen storage disease are reported. The author did not find the blood sugar curves following administration of dextrose, epinephrine or insulin satisfactory for differentiating this condition from fatty liver or hepatic cirrhosis. He did find a distinct difference in response to the administration of dioxyacetone. In glycogen storage disease most of this substance is transformed rapidly to sugar or glycogen, whereas in the other forms of hepatic injury it is formed in high concentrations in the blood. He believes that, although some children who present a liver surcharged with glycogen may recover, others, as a result of infections or other nocive influences, may come to have fatty liver or fatty cirrhosis of the liver.

LESLIE, Evanston, Ill.

CHYLOUS CYSTS IN THE FIRST WEEKS OF LIFE. KLEIN, Jahrb. f. Kinderh. **148**: 223 (Jan.) 1937.

Vomiting was the characteristic symptom in the subject. It started just before the age of 5 weeks. A soft cystic mass was found in the lower part of the abdomen. On laparotomy, chylous cysts were found and removed. Because of complications, the child had to be operated on twice more and eventually died.

LANDAU, Hannibal, Mo.

ACTION OF PROSTIGMINE IN PARALYTIC ILEUS OF INFANTS. T. ROHLEDER, Kinderärztl. Praxis **10**:115 (March) 1939.

Rohleder describes 4 cases of paralytic ileus in which the injection of 0.2 to 0.3 cc. of prostigmine had a convincing influence in a short time. The condition occurred in 1 patient after an abdominal operation; in another, an atrophic infant, it occurred in spells, and in 2 infants it accompanied alimentary intoxication.

HEYMANN, Cleveland.

ATYPICAL PYLOROSPASM. E. GRASER, Kinderärztl. Praxis **10**:159 (April) 1939.

The use of conservative therapy for vomiting in 2 infants is described. The vomiting was not projectile, however, and the treatment used failed to improve

the condition. No tumor of the pylorus was felt; no peristaltic waves were seen. Operation, however, was performed and revealed a hypertrophic pyloric muscle in both cases.

HEYMANN, Cleveland.

INTRAMESENTERIC DIVERTICULUM OF THE SMALL INTESTINE. J. MELLGREN, Virchows Arch. f. path. Anat. **302**:677, 1938.

A 15 cm. long intramesenteric diverticulum of the small intestine furnishes the basis of a thorough review of the literature relating to diverticula of this type and a discussion of the theories advanced to explain their occurrence. Characteristic of such a diverticulum is its intramesenteric situation, its relative length, its gross and microscopic similarity to the normal intestine and its blind ending. In the author's opinion, this type of diverticulum is derived from the omphalomesenteric duct, but additional abnormality of development of the first part of the intestine must occur to account for its intramesenteric situation.

SCHULTZ, Chicago. [ARCH. PATH.]

RUPTURE OF THE STOMACH BY FERMENTATION OF THE CONTENT OF THE STOMACH. J. H. LICHTENBELT, Nederl. tijdschr. v. geneesk. **83**:1340 (March 25) 1939.

A boy aged 14 years had a spontaneous rupture of the stomach as a result of fermentation and the resultant accumulation of gas. The abdomen was markedly distended, with compression of the blood vessels and consequently no circulation in the legs, leading to severe pain. It is possible that the pylorus was kept closed for too long a time by an injection of 10 mg. of morphine hydrochloride. Subcutaneous emphysema developed one hour after death.

VAN CREVELD, Amsterdam, Netherlands.

LIVER FUNCTION TEST OF QUICK. G. A. LINDEBOOM, Nederl. tijdschr. v. geneesk. **83**:1734 (April 15) 1939.

Lindeboom reports experiences with Quick's liver function test. This test is based on the synthesis of hippuric acid from benzoic acid and aminoacetic acid. Conditions in which the test reveals disturbances are, next to renal lesions with retention of nitrogen, a large variety of hepatic disturbances (obstructive jaundice, cardiac engorgement of the liver, hepatitis, cirrhosis). The diagnostic and the differential diagnostic value of the test are discussed.

VAN CREVELD, Amsterdam, Netherlands.

ILEUS CAUSED BY A PIECE OF DRIED APPLE. H. J. POSTEL, Nederl. tijdschr. v. geneesk. **83**:1960 (April 29) 1939.

Postel records a case of very slowly progressive intestinal occlusion caused by the swelling of an undigested piece of dried apple.

VAN CREVELD, Amsterdam, Netherlands.

Nervous Diseases

MENTAL CHANGES IN CHOREA MINOR. D. SHASKAN, Am. J. Psychiat. **95**:193 (July) 1938.

Thirty-five cases of chorea minor were studied, especially from the standpoint of mental changes. The cases were accordingly divided into the following three groups: (1) chorea with severe psychosis, 8 cases (in 2, in addition to psychosis there was severe carditis); (2) chorea with mild mental disturbance, 9 cases, and (3) chorea without gross mental changes, 16 cases.

This study suggests that severe mental symptoms associated with chorea, such as were observed in the first group, indicate a grave prognosis. In this group,

atypical motor signs, such as flaccidity and tonic and rhythmic phenomena, were frequent. While fever therapy proved beneficial in the milder forms, in the severe forms it was ineffective.

The mental changes are closely connected with disturbances in impulse. Symptoms of emotional instability, such as increased laughing and crying, predominate. Though disturbances in behavior may become a serious problem in the milder forms, orientation and thinking remain clear.

JAHR, Omaha.

SUBDURAL HEMATOMA: DIAGNOSIS AND TREATMENT. P. A. KUNKEL and W. E. DANDY, Arch. Surg. **38**:24 (Jan.) 1939.

Subdural hematoma is usually the result of trauma. In 17 cases of the authors' series of 48 cases no history of even a trivial injury could be elicited. The principal symptoms of subdural hematoma are those of intracranial pressure. The most common symptoms in the order of frequency are headache, drowsiness, nausea or vomiting, vertigo, diplopia and mental confusion. Without the history of trauma the diagnosis is difficult, because the findings do not differ from those produced by any intracranial space-occupying lesion. When the diagnosis cannot be made from the symptoms and signs, a precise localization can be made by ventriculographic study. A small craniotomy opening with evacuation of the hematoma is the operation of choice. In the authors' series there was a case mortality of 4 per cent.

KAISER, Rochester, N. Y.

LYMPHOCYTIC CHORIOMENINGITIS: A DISCUSSION OF ITS DIAGNOSIS IN MAN. M. E. HOWARD, J. Infect. Dis. **64**:66 (Jan.-Feb.) 1939.

Howard reports a case of benign lymphocytic choriomeningitis in which the virus was isolated from the spinal fluid about the sixth or seventh day after the infection started, i. e., about the time when the cellular response in the spinal fluid was highest. Neutralizing antibodies of low titer were demonstrated in the patient's serum. The virus lost its activity in guinea pigs during constant passage through mice.

TOOMEY, Cleveland.

TONIC NECK REFLEX IN THE HUMAN INFANT: MORPHOGENETIC AND CLINICAL SIGNIFICANCE. A. GESELL, J. Pediat. **13**:455 (Oct.) 1938.

Magnus in his classic work on *Körperstellung* (body posture) reported an analysis of the postural reaction of the decerebrate quadruped when the head was experimentally turned to an extreme right or left position. The response found was an extension of the forelimb on the side toward which the head was turned and flexion of the opposite forelimb. Magnus expressed the belief that in man the tonic reflex is a pathologic phenomenon. Gesell, however, has found that the tonic neck reflex is a normal and virtually universal feature of the normal neonatal infant, spontaneously manifested when the infant is in the supine position; that for eight weeks the reflex holds sway, at twelve weeks is less conspicuous, at sixteen weeks is in transition and at twenty weeks is in eclipse, for at twenty weeks 100 per cent of the normal infants whom he observed maintained the head in midposition. Marked persistence of the tonic neck reflex beyond the first half year is indicative of retarded, arrested or defective development. In association with evidence of lesions of the basal ganglions it is an indication that the child will not "learn" to walk.

RAUH, Cincinnati.

POLYNEURITIS IN CHILDREN. R. E. CUTTS, Minnesota Med. **22**:89 (Feb.) 1939.

Cutts was requested to make a résumé of cases of polyneuritis in children, with a view to determining the efficacy of vitamin B in this condition, owing to the flood of publications concerning the matter. He found a low incidence of polyneuritis among the children of Minnesota, as judged by the records of the

University Hospital, but he feels that the condition is important because of the prolonged and severe disability resulting from it. He discusses the gross pathologic features, the symptoms, the causes and the prognosis and briefly cites 8 cases of varied origin. He concludes that, while up to the present the giving of vitamin B has been impracticable, the fact that the vitamin is now available in pure concentrated form will speed the determination of its value. The giving of nicotinic acid has been shown to be ineffective in the treatment of polyneuritis.

ANDERSON, Minneapolis.

BENIGN LYMPHOCYTIC MENINGITIS. D. A. CANNON, Glasgow M. J. **13**:1 (Jan.) 1939.

Cannon described 4 cases in which there was an increase in the spinal fluid cell count, practically all the cells being lymphocytes. The clinical features were: acute onset with fever and evidence of meningeal irritation; changes in the spinal fluid, such as increased pressure, increase of cells (mainly lymphocytes), a normal chloride content, and absence of organisms. The clinical course was uniformly benign, with no complications. There was no associated systemic or local infection. Many names have been suggested, and certain investigators have been able to isolate a virus from similar cases.

SNELLING, Toronto, Canada.

HEMORRHAGE OF THE BRAIN STEM AS A SIGNIFICANT COMPLICATION OF INTRACRANIAL TUMORS. L. B. COX, M. J. Australia **1**:259 (Feb. 18) 1939.

Cox observes that hemorrhage of the brain stem is of common occurrence in cases of intracranial tumor situated above the tentorium cerebelli. It was found at autopsy in 10 of 49 cases of supratentorial tumor and in 1 case of subdural hematoma. It was not observed in 25 cases of tumor of the posterior fossa. Although signs that might indicate with certainty the position in which these hemorrhages occur are not usual, coma of sudden onset or confusion developing over a few hours may be present. The reason for the occurrence of hemorrhage of the brain stem in association with both supratentorial hemorrhage and tumor cannot yet be stated with certainty.

GONCE, Madison, Wis.

SEROUS MENINGITIS OF OTITIC ORIGIN; DECOMPRESSION TREPHINING; CURE AFTER SEVERE PROLONGED MALNUTRITION. H. GRENET and P. ISAAC-GEORGES, Bull. Soc. pédiat. de Paris **36**:582 (Oct.) 1938.

In a 10 month old boy otitis media developed following pertussis. There were repeated periods of fever, characterized by flaring up of the otitis each time. The cell count of the spinal fluid was high, but no micro-organisms were found in smear or culture. Bilateral papilledema was noted. It was thought that the patient might have a cerebral abscess. In the absence of any ventriculographic abnormalities a diagnosis of serous meningitis was made. A right subtemporal decompression was performed. The boy recovered but severe malnutrition developed as a result of obstinate anorexia. Examination of gastric juice revealed hypochlorhydria. He was given a preparation of hog gastric juice. The appetite improved thereafter, and he began to gain weight.

BENJAMIN, Montreal.

ENCEPHALOGRAPHIC AND VENTRICULOGRAPHIC EXPERIENCE WITH CHILDREN. R. STANKIEWICZ and M. KOWALEWSKI, Rev. franç. de pédiat. **14**:322, 1938.

Ninety cases of disease of the brain or of the meninges were studied by this method from the point of view of diagnosis and from that of therapy. Particularly good results were obtained in cases of epidemic meningitis and of jacksonian epilepsy, in which, the authors believe, the air and subsequent movement of cerebrospinal fluid was efficacious in breaking up adhesions. Roentgen radiation was used in addition when it seemed desirable to reduce the formation

of cerebrospinal fluid, as in some cases of hydrocephalus. The authors are enthusiastic, and they present their material in a thorough manner. The illustrations are excellent.

LESLIE, Evanston, Ill.

PATHOLOGY OF THE SUPERIOR LONGITUDINAL SINUS IN THE SUCKLING. F. PONTIERI, Med. ital. **1**:17 (Jan.) 1939.

Five cases of thrombosis of the superior longitudinal sinus are presented. The anatomy and the numerous malformations are pointed out. The causes of thrombosis are discussed. The symptom complex and the changes in the spinal fluid are presented. An explanation of these changes is given.

MARTOCCIO, Brooklyn.

CHOREA MINOR AND SEASON. H. PETERS, Ztschr. f. Kinderh. **60**:515 (Feb. 18) 1939.

A study covering a thirty year period revealed that the incidence of chorea is definitely higher during the winter and spring months. Peters discusses possible etiologic factors. Apparently there is a parallelism in the incidence of chorea and rheumatism.

SIEMSEN, Chicago.

CARE OF EPILEPTIC PATIENTS IN SWEDEN. A. PETRÉN, Svenska läk.-sällsk. förhandl., May 31, 1938, p. 310.

The Swedish parliament has decided to erect two institutions for the observation and treatment of epileptic patients, one for mentally normal children and women and the other for men.

WALLGREN, Göteborg, Sweden.

CEREBELLAR FORM OF SATURNINE ENCEPHALOPATHY. A. BIEMOND and S. VAN CREVELD, Nederl. tijdschr. v. geneesk. **83**:16 (Jan. 7) 1939.

A cerebellar form of lead encephalopathy was observed in a girl 2 years old, caused by the use of drinking water containing lead. During twelve months after the first appearance of the neurologic symptoms, these symptoms gradually improved. Attention is drawn to the peculiar character which lead poisoning in childhood often shows. Basophilic stippling and polychromasia were lacking in the case described. Some recent views on the diagnosis and therapy of lead poisoning are communicated.

FROM AUTHORS' SUMMARY.

Psychology and Psychiatry

STUDIES IN MONGOLISM: III.—PITUITARY BODY. CLEMENS E. BENDA, Arch. Neurol. & Psychiat. **42**:51 (July) 1939.

The author studied, pathologically, the pituitary glands of 14 mongoloid patients. In 13 of the cases there were pathologic changes consisting of an increase in the eosinophilic cells and a deficiency of the basophilic and chief cells. This deficiency seems to be characteristic of mongolism.

"There are many indications that mongolism is the result of a morphologic failure and is due to an endocrine disturbance. The key to the general disorder seems to be a particular pituitary deficiency which may be due to a pituitary deficiency in the mother during pregnancy."

BEVERLY, Chicago.

ONYCHOPHAGY. JOSEPH SCHWARTZMAN, Arch. Pediat. **56**:599 (Sept.) 1939.

Nail biting in children occurs more frequently than is usually considered. It is not a mental abnormality or a stigma but rather a barometer of the nervous system's lowered threshold to stress. Although it may be considered a temporary

manifestation with a tendency to disappear in adult life, it may have deleterious effects on the body, and therefore attempts to curtail it should be made. Removal of the cause if possible, reeducation of the child and constant encouragement and cooperation are essential to effective results.

ORR, Buffalo.

PSYCHOSES IN CHILDREN. IRENE C. SHERMAN, Illinois M. J. **75**:446 (May) 1939.

According to Sherman's studies, the number of children who become psychotic is relatively small. There is, however, she believes, a great need for standardization of ideas as to what constitutes a psychosis in a child. With children it is particularly difficult to distinguish between behavior problems and definite mental abnormalities. When a child has a psychosis, the way the illness expresses itself will depend on the characteristic he has developed, and this necessarily varies with his age and experience.

BARBOUR, Peoria, Ill.

THE PEDIATRICIAN AND THE EMOTIONALLY DISTURBED CHILD. WILLIAM S. LANGFORD, M. Clin. North America **23**:715 (May) 1939.

Well over half of the pediatrician's patients are affected by some emotional disturbance. The importance of the parent-child relation in the genesis of these disturbances must be understood if such conditions are to be properly evaluated and successfully handled. This is especially true in early childhood, while the child's horizons have not yet extended beyond the home. The child-mother relation at this period is of the greatest immediate importance. In this paper Langford discusses in particular the problems of the intelligent mother who in her zeal to prepare herself to rear her child properly devours the latest literature on child psychology and endeavors to put into practice in her home the often diametrically opposed ideas which she has partially absorbed. Every contact with her child is consciously planned, as a result of which the normal spontaneous mother-child relation is lost. The child senses the mother's mental insecurity and reacts with various mental and emotional disturbances. The first step in the adjustment of these difficulties is to uncover, if possible, the underlying causes of the maternal attitudes. This may require considerable time and skill but is essential to the solution of the problems. In the case of the young child it may be feasible to attempt only to deal with these environmental conditions and to rely on the inherent factors of growth and development to enable him to overcome his difficulties. The varied elements which may enter into such a problem, involving both maternal and paternal attitudes, is illustrated by a detailed case history.

EUGENE H. SMITH, Ogden, Utah.

THE INFERIORITY COMPLEX AND ITS CURE. S. COBB, Proc. Conf. Educ. & Exceptional Child, May 1938.

Cobb emphasizes the need for progressive education in dealing with children, especially those who are mentally retarded and have feelings of inferiority. By "progressive education" he means an educational program developed for the individual child—small classes and teachers who understand the needs of each pupil. He states that retardation may be on a physical, psychologic or emotional basis.

BEVERLY, Chicago.

NEED OF SPECIAL EDUCATION FOR THE EXCEPTIONAL CHILD. K. M. COOK, Proc. Conf. Educ. & Exceptional Child, May 1938.

The general problem of the handicapped child is discussed from the educational standpoint. Mrs. Cook indicates the need for federal aid in securing care and training for these children.

BEVERLY, Chicago.

THE SOCIAL ADJUSTMENT OF THE EXCEPTIONAL CHILD OF BORDERLINE MENTALITY. M. MURPHY, Proc. Conf. Educ. & Exceptional Child, May 1938.

From statistical studies of inmates of correctional institutions, Murphy concludes: 1. Foster homes furnish a higher proportion of delinquents than child-caring institutions. 2. Delinquents, no matter where they have lived, have the same number of offenses charged against them. 3. No matter what type of residence the child comes from, it seems to be advantageous for him to stay longer in the correctional institution.

It is certainly not apparent from these conclusions that placement in foster homes is more advantageous than placement in home-caring institutions.

It should be emphasized that the author drew these conclusions from the statistics alone and did not consider the emotional problems other than delinquency in the various groups of children.

BEVERLY, Chicago.

PROGRESSIVE EDUCATION CONSIDERS THE EXCEPTIONAL CHILD. W. C. RYAN JR., Proc. Conf. Educ. & Exceptional Child, May 1938.

Ryan emphasizes the need for consideration of the growth and development of human beings in school rather than external organization, grades and the mechanisms of education of the past.

BEVERLY, Chicago.

NATURE AND IMPLICATIONS OF TRUANCY FROM THE STANDPOINT OF THE SCHOOLS. J. E. W. WALLIN, Proc. Conf. Educ. & Exceptional Child, May 1938.

Juvenile truancy may be (1) the expression of the normal curiosity of every child to explore or (2) a mechanism of escape from an intolerable situation. In either case there results a personal maladjustment which leads to a harmful habit pattern. This fosters an attitude of refusing to accept responsibility or authority.

In discussing the prevention of truancy Wallin considers first the maladjusted school teacher and second the maladjusted or ill adapted curriculum. The majority of truants are children who are unable to follow the school program.

BEVERLY, Chicago.

THE CORRELATION BETWEEN THE PEDIATRIST, PSYCHIATRIST AND PSYCHOLOGIST. W. B. MCILWAINE, Virginia M. Monthly **66**:96 (Feb.) 1939.

The author cites cases of emotional disturbances occurring in adolescents and stresses the importance of proper treatment of the mental state as well as of associated physical disorders in order to prevent the development of more serious mental disorders. When mental or emotional disturbances are diagnosed, salvage may depend on the cooperative efforts of the family, the physician, the psychologist and the psychiatrist.

STONE, Richmond, Va.

JUVENILE DELINQUENCY. JOHN MCGEORGE, M. J. Australia **2**:94 (July 15) 1939.

This paper is concerned with major delinquencies, which may be defined as antisocial acts or offenses punishable by law.

Etiology.—Undoubtedly the most important environmental influence is the home. Five types of homes are listed as being bad environmental influences: the slovenly home, the repressive home, the indulgent home, the broken home and the indifferent home where bad companionship and lurid literature take the place of parental affection. Other environmental factors include hero worship when the hero is unfortunately not worth emulation. Fear may readily lead to excessive lying and to stealing.

Physical factors are of less importance than environmental factors, but complete examination should be made of all children.

Mental factors may be listed under three groups: (1) the normal delinquent whose crime was committed in extreme circumstances; (2) nonpsychopathic

personality deviates, including the neurotic, schizoid or paranoid types; (3) definite psychopathic personalities.

Mental testing is of great importance in determining mental deficiency.

Symptoms.—Stealing, persistent lying, truancy and sex offenses are the outstanding manifestations of delinquency.

Treatment.—"The keynote of success in dealing with delinquents is genuine understanding of the problems which have suddenly confronted a child, incapable, through no fault of his own, of solving them." TENNEY, Madison, Wis.

THE DIFFICULT CHILD. D. W. H. ARNOTT, M. J. Australia **2**:105 (July 15) 1939.

The importance of mental deficiency from various causes in producing difficulties in behavior is shown by reports of several cases. TENNEY, Madison, Wis.

EDUCATION AND SOCIAL ADAPTATION OF WAYWARD MINORS OR OF THOSE IN DANGER OF BECOMING SO. LUIS MORZONE, Bol. Inst. internac. am. de protec. a la infancia **12**:417 (Jan.) 1939.

This is a plea for facilities for special study and education of children showing a tendency to criminal activity. LESLIE, Evanston, Ill.

JUVENILE FORM OF AMAUROTIC IDIOCY. G. TAMÁSI and I. ZIMÁNYI, Kinderärztl. Praxis **10**:357 (Aug.) 1939.

The authors survey the literature on the subject and describe a case in which a tentative diagnosis was made. As the typical "cherry spot" is not present in the juvenile form and the disease is observed in children of non-Jewish descent, the authors did not feel certain of their diagnosis. No biopsy specimen from the lymph nodes, spleen, bone marrow or brain was examined, nor was a postmortem examination made to support the diagnosis. HEYMANN, Cleveland.

Diseases of the Genitourinary Tract

PREPUTIAL ADHESIONS IN THE CIRCUMCIZED PENIS. M. B. MARKS, Arch. Pediat. **56**:458 (July) 1939.

The subject is discussed. ORR, Buffalo.

MANAGEMENT OF URINARY INFECTIONS IN INFANTS AND CHILDREN. M. F. CAMPBELL, M. Clin. North America **23**:669 (May) 1939.

Urinary infections are even today loosely, inadequately and often incorrectly designated as pyelitis. The usual lesion, however, is suppurative pyelonephritis. It would be more accurate to designate those conditions the anatomic diagnosis of which is uncertain simply as pyuria until their nature is determined.

An acute urinary infection in childhood is usually abrupt in onset, with chills, fever and vomiting. Enteric disturbances and neurologic manifestations are common. Loin or renal pains or tenderness may be present. Symptoms directly referable to the urinary tract are strangely lacking in a fourth or a third of patients with chronic pyuria. The urine of every child sick from any cause should be examined.

The seriousness of acute urinary infection in children is suggested by the mortality of 20 to 40 per cent of young infants with this condition and approximately 3 per cent of older children with it.

The general treatment of patients with acute urinary infections is important. Maintenance of nutrition merits first consideration. Rest in bed is important until

after the temperature becomes and remains normal. No special diet is indicated. Large amounts of dextrose assist in the reduction and control of acidosis. The bowels should be kept open, and colonic irrigations are extremely useful in detoxifying the patient. Alkalinization of the urine brings about striking symptomatic improvement but does not combat the infection. Campbell's first choice as a urinary antiseptic is mandelic acid, recourse being had to sulfanilamide when this fails. Alternate use of these two drugs may be of benefit in resistant conditions. In the hyperacute stage medication by mouth is withheld until the child becomes stabilized as to alimentation, acidosis and fluid balance. The indications and limitations of these drugs are fully discussed. The results of treatment should be checked by bacteriologic tests of the urine after the drugs have been discontinued for three to four days. A patient should be pronounced cured only after two cultures have proved negative.

Should chemotherapy fail after four weeks' trial, careful study will usually disclose that stasis is present, requiring instrumental or urosurgical treatment.

SMITH, Ogden, Utah.

GYNANDROID MACROGENITOSOMIA. E. SORREL, SORREL-DEJERINE and DE LARMINAT, Bull. Soc. pédiat. de Paris **37**:66 (Feb.) 1939.

A girl 8½ years old had the body build, genital development and pubic hair of a normal girl of 15 years. The epiphyses of the long bones were consolidated. She presented no signs of tumor of the brain, adrenals or ovaries. She was the subject of a previous report when she was 4 years old. At that time she was operated on, and it was established that she possessed a uterus and two ovaries; there was no evidence of testicles. A vagina was reconstructed, and a large clitoris, resembling a penis, was left intact. She now showed some evidence of hermaphrodism, having some male characteristics, such as hair on the upper lip, a prominent larynx and a deep voice. Assays of the urine for androgenic substances were to be carried out. It was noted that her general development was accelerated when she was a year old.

BENJAMIN, Montreal, Canada.

PASSAGE OF RED BEET PIGMENT IN URINE. J. CATHALA, JÉQUIER, P. MARTROU and L. GRAS, Bull. Soc. pédiat. de Paris **37**:88 (Feb.) 1939.

The presence of beet pigment in urine is connected with hyperacidity of the urine. The usual normal urinary p_H is 6.2. A boy 4½ years old was supposed to have hematuria. The red coloration of the urine followed the eating of beets. The urine acted as an acid base indicator, being red when strongly acid and yellow when alkaline. Beet juice reacted similarly. In 2 of 3 children in whom preliminary hyperacidification of the urine to p_H 4.4 had been accomplished by means of a ketogenic diet, calcium chloride and phosphoric acid, ingestion of cooked beets was followed by some reddish pigmentation of the urine. It appears that normally the pigment is changed to colorless constituents, but that in certain children acidity prevents the destruction of the beet pigment in the body. This pigment belongs to the group of anthocyanosides.

BENJAMIN, Montreal, Canada.

FACTORS IN NOCTURNAL ENURESIS. J. WERTHEIMER, Rev. franç. de pédiat. **14**: 264, 1938.

In observations on 30 infants Wertheimer found that an infant always awakens before urinating; also that urination is less frequent when the infant is in the ventral than when it is in the dorsal position. Four children were treated for enuresis by maintenance of the ventral position. The results were satisfactory.

LESLIE, Evanston, Ill.

PYELONEPHRITIS IN INFANCY FROM CONGENITAL MALFORMATIONS OF THE KIDNEY. F. SALA, G. CARDELLE and J. PEREIRA, Arch. de med. int. **4**:5, 1939.

The anomalies of the kidney that may cause pyelonephritis are divided into anomalies of number, form, structure, size, localization, rotation, renal pelvis and blood supply. Examples are given with photographs of the anomalies as observed at autopsy and photomicrographs. Such conditions may almost be discovered by means of pyelograms of the urinary tract. In the face of such anomalies, treatment is not very encouraging. An excellent bibliography is appended.

SANFORD, Chicago.

CAUSE, GENESIS AND RESULTS OF NEPHRITIS IN CHILDREN. E. HINZE, Jahrb. f. Kinderh. **148**:177 (Jan.) 1937.

One hundred and twenty-eight children with nephritis were observed over a period of ten years. Nephritis following sore throat led with an incidence of 26.6 per cent, followed by postpyodermic nephritis with an incidence of 14.8 per cent.

Ninety-eight children had true glomerulonephritis, 12 true nephrosis, 4 interstitial nephritis and 4 pyelonephritis. One child had embolic focal nephritis. There were 7 children with tuberculosis of the kidney.

In 58.7 per cent of the patients the lesions healed completely; in 13.95 per cent they showed a chronic tendency.

The general mortality rate was 19 per cent; 5.8 per cent died during the acute illness or with an intercurrent infection; 4.1 per cent died during the acute episode, and 9 per cent died during the chronic phase.

The course of nephritis following a sore throat is favorable. The average healing period in this series was seven weeks.

Postscarlatinal nephritis ordinarily carries a good prognosis. In this series the average day of onset of the nephritis was the eighteenth day of the scarlet fever.

LANDAU, Hannibal, Mo.

Diseases of the Ductless Glands; Endocrinology

EFFECT OF ZINC ON INSULIN AND ITS MECHANISM. M. SAHYUN, Am. J. Physiol. **125**:24 (Jan.) 1939.

Zinc in the amount of 2 mg. or more per thousand units of insulin augments to a pronounced degree the physiologic effect of insulin. The prolongation of the action of insulin by zinc is probably due to the adsorption of insulin protein on insoluble basic zinc salts. Insulin protein is adsorbed on basic zinc salts at about neutrality.

NOURSE, Cleveland.

PERSISTENT DIABETES FOLLOWING THE INJECTION OF ANTERIOR PITUITARY EXTRACT. F. C. DOHAN and F. D. W. LUKENS, Am. J. Physiol. **125**:188 (Jan.) 1939.

Persistent diabetes was produced in 3 of 8 dogs by progressive larger doses of anterior pituitary extract. While the intensity of the diabetes varied, the metabolic behavior of the animals was similar to that of partially depancreatized dogs. Histologic evidence indicated damage to the islands of Langerhans.

NOURSE, Cleveland.

HYPERPARATHYROIDISM PRODUCED BY DIET. E. J. BAUMANN and D. B. SPRINSON, Am. J. Physiol. **125**:741 (April) 1939.

Hyperparathyroidism has been produced in rabbits by feeding them a diet low in calcium and high in phosphorus. This diet causes enlargement of the parathyroids to two or more times their normal size, with hypertrophy of the cells and nuclei and an increase in the amount of lipids in the cytoplasm. Serum

calcium and phosphorus are low but within the normal range, while serum phosphatase is possibly lower than normal. Aside from increased vascularity, no important changes were found regularly in the bones. The value given by the Hamilton and Schwartz test for parathyroid hormone was always high.

NOURSE, Cleveland.

HYPOTHALAMIC-PITUITARY SYNDROMES. L. LICHTWITZ, Bull. New York Acad. Med. **15**:773 (Dec.) 1939.

This paper offers an epitome of the functions of the hypothalamus with special reference to the physiologic and clinical phases of the strange syndromes known as diabetes insipidus, infantile gigantism and dystrophia adiposogenitalis. To appreciate the discussion, one must read the article in the original. This is well worth the time of any physician interested in these problems.

JAHR, Omaha.

THYMIC ASTHMA. W. M. WHITEHEAD, Northwest Med. **38**:387 (Oct.) 1939.

Whitehead believes that there are three types of abnormality caused by hyperplasia of the thymus: (1) thymic stridor, (2) thymic asthma and (3) thymicolymphaticus.

He reports the case of a 13 month old girl with difficult respiration, unrelieved by epinephrine, inhalants or morphine. The condition was relieved by ice packs applied to the neck and upper part of the chest for five hours. There was a return of the symptoms with each "cold," but treatment with ice again brought relief.

ROBERTSON, Omaha.

ATROPHIC AND LIPOMATOUS LIPODYSTROPHY AFTER REPEATED INJECTIONS OF INSULIN IN TWO DIABETIC CHILDREN. P. NOBÉCOURT and P. DUCAS, Bull. Soc. pédiat. de Paris **36**:644 (Nov.) 1938.

Two diabetic children who had been receiving injections of insulin for several years were presented. One had numerous subcutaneous lipomas, and the other showed areas of atrophy of subcutaneous fat in regions where repeated injections had been made. Theories as to the cause of these abnormalities of subcutaneous fat are mentioned, including the theories that the condition results from trauma, small hemorrhages or the lipolytic action of preservative fluid, such as tricresol; but the authors say that experimental evidence does not substantiate the theories. The cause of lipodystrophy associated with injections of insulin is at present obscure. The only known way to reduce it to a minimum is to change the site of injection as often as possible so that the same spot is not used repeatedly at short intervals.

BENJAMIN, Montreal, Canada.

RESULTS OF THE USE OF PROTAMINE ZINC INSULIN IN THE TREATMENT OF DIABETES IN CHILDREN. P. NOBÉCOURT, P. DUCAS and LAROCHE, Bull. Soc. pédiat. de Paris **36**:649 (Nov.) 1938.

Eight diabetic children who were receiving injections of ordinary insulin were gradually placed on a regimen which was controlled by a single injection of protamine zinc insulin each morning. It took only a few days after the change was made for the patients gradually to begin to utilize the latter type of insulin from one injection each twenty-four hours as adequately as they had utilized a similar amount of ordinary insulin divided into three injections, one before each meal.

BENJAMIN, Montreal, Canada.

GOITER ACQUIRED AT HAUTE-SAVOIE. M. OMBRÉDANNE and LE JEMBLE DE LA HUSSAIRE, Bull. Soc. pédiat. de Paris **37**:104 (Feb.) 1939.

Goiter and symptoms of thyrotoxicosis developed in two brothers, 9 and 11 years old, after they had spent about a year at Haute-Savoie, France, where

goiter is known to be endemic. Rapid improvement accompanied the administration of 2 drops of iodine solution three times daily for two months.

BENJAMIN, Montreal, Canada.

THE ADRENAL IN THE NUTRITIONAL DISTURBANCES OF INFANTS. A. VON SZASZ, Monatschr. f. Kinderh. **79**:332, 1939.

This is a report of 4 cases of severe nutritional disturbance, in 2 of which autopsy showed the adrenals involved by hemorrhage. Two patients recovered. An extract of the adrenal cortex was used in treatment, and the writer believes it was of value.

GERSTLEY, Chicago.

SIMMONDS' DISEASE IN CHILDHOOD. J. GELDRICH, Monatschr. f. Kinderh. **80**:103, 1939.

Progressive emaciation in a child ended in death when the child reached the age of 14 years. The striking features were loss of weight, progressive weakness, marked anorexia, hypotonia, subnormal temperature, oliguria, low metabolism and disturbances in carbohydrate metabolism, such as hypoglycemia and a diabetic sugar tolerance curve. Against a diagnosis of Addison's disease were the absence of pigmentation, of dehydration and of changes in the blood chlorides and a negative tuberculin reaction.

The report loses much in that the child died with symptoms of cardiac insufficiency and no autopsy was obtained.

GERSTLEY, Chicago.

Diseases of Muscles, Bones, Joints and Lymph Glands

RELATIONSHIP OF MAXILLARY AND MANDIBULAR GUM PADS IN THE NEWBORN INFANT. J. H. SILLMAN, Am. J. Orthodontics **24**:409, 1938.

A careful study of the relationship of the maxillary and mandibular gum pads was made in 709 newborn infants. The ages ranged from 1 to 11 days. In order to determine accurately the relationship of the gum pads, casts had to be made and articulated by a bite. The following observations were made: The gum pad of the mandible is distal to that of the maxilla in all cases on an average of 2.7 mm. in the male and 2.5 mm. in the female. The range of variation of this distal relationship is from 0 to 7 mm. There is a limited anteroposterior movement of the mandible but no lateral movement. When the jaws are at rest, the gum pads do not meet. The space between the anterior segments of the gum pads varies in form. With an increase in the distal relationship of the jaws, the dimensions of the mandibular gum pads seem to be affected; the length and anterior width show an increase, while the posterior width shows a decrease. A comparison between spontaneously delivered babies and those delivered instrumentally shows little difference in the dimensions of the gum pads. Babies delivered by elective cesarean section compared with those born in face presentation do, however, show appreciable dimensional differences.

FROM AUTHOR'S SUMMARY.

PHARMACOTHERAPY OF CHRONIC RHEUMATISM. J. F. HALLS DALLY, Brit. J. Phys. Med. **1**:379 (Nov.) 1938.

The article is a critical discussion of various drugs used in the treatment of chronic rheumatism. The author discusses the indications, mode of action, dosage and results of the use of more than thirty drugs. He also considers the use of external applications, vaccines and nonspecific protein therapy. He believes that vaccines are most beneficial for young patients with recent manifestations of the disease.

HARTMAN, Cleveland.

OSTEOMYELITIS OF THE SPINE OF THE SCAPULA. N. BARBILIAN and E. REPCIUC, Bull. Soc. de pédiat. de Iasi **7**:43 (Jan.-June) 1937.

A patient had severe pain in the left shoulder and fever following exposure to cold, succeeded by a discharge of pus in the region of the left axilla. Four weeks later a roentgenogram showed marked destruction of the spine of the scapula. This was removed at operation. Recovery occurred, with a fair degree of mobility of the arm.

LESLIE, Evanston, Ill.

A CASE OF LYMPHOBLASTOMA. ROBERT DEBRE, ROEDERER and M. L. JAMMET, Bull. Soc. pédiat. de Paris **36**:463 (July) 1938.

A boy 6½ years old had multiple tumors, especially of the skull and other bones. Biopsy revealed the presence of round cell sarcoma which may have been lymphoblastoma. He became extremely cachectic and died about five months later.

BENJAMIN, Montreal, Canada.

ISOLATED RUPTURE OF THE LESSER TROCHANTER IN THE EPIPHYSIAL LINE: A TYPICAL "SPORT INJURY" OF YOUTH. K. HERZOG, Deutsche Ztschr. f. Chir. **251**:449 (Jan.) 1939.

The lesser trochanter, from the time of appearance of the center of ossification at 9 years to its bony union with the femur at 18 years, may be avulsed by the pull of the iliopsoas muscle during violent exercise. The signs—local tenderness, swelling in the iliopectineal fossa, tendency to outward rotation and difficulty in raising the thigh—are confirmed by roentgen examination. A flexed, slightly externally rotated position of the thigh should be maintained for two weeks. Callus formation occurs in four weeks, and healing is generally uneventful.

HARRIS, Durham, N. C.

FETAL CHONDRODYSTROPHY AND CONGENITAL SYPHILIS. M. KLEIN and F. GOLDMANN, Jahrb. f. Kinderh. **148**:213 (Jan.) 1937.

A case of fetal chondrodystrophy associated with congenital syphilis is described. Characteristic lesions of both conditions are seen in the accompanying roentgenograms of the long bones.

LANDAU, Hannibal, Mo.

OSTEODYSTROPHIA FIBROSA OF THE FACIAL BONES. K. HELLMANN, Monatschr. f. Ohrenh. **73**:40 (Jan.) 1939.

The author describes 4 cases of osteodystrophia fibrosa of the facial bones, but no illustrations accompany the article.

CASE 1.—A boy of 16 had a swelling in the left cheek. Roentgen examination revealed a tumor within the left maxillary sinus. The tumor was grown together with the floor of the orbit. A Caldwell-Luc operation was performed, with recovery.

CASE 2.—A youth of 18 had a thickening of the right frontal bone and the right superior maxilla. Roentgen examination showed that the right frontal and the right maxillary sinus were filled with a sclerotic bony tumor. Parts of the tumor were removed.

CASE 3.—A woman of 21 had a tumor as big as the head of a child in the region of the cheek. At operation a big cyst was found, displacing the maxillary sinus and the ethmoid bone.

CASE 4.—The patient had a swelling as big as an apple in the left cheek. At operation a tumor was found, containing many cysts.

LEDERER, Chicago. [ARCH. OTOLARYNG.]

IRITIS IN BESNIER-BOECK-SCHAUMANN DISEASE. G. ÖSTERBERG, Nord. med. tidskr. **16**:1125 (July 16) 1938.

This paper is a report of a case of benign lymphogranulomatosis in a girl aged 14. The main symptoms and signs were gradually developing, almost painless nodules at the periphery of the iris, encroaching on the cornea, which was almost perforated in several places. There was no glaucoma. Vision was reduced to 2/60. The tuberculin reaction was positive. A roentgenogram of the lungs showed a picture resembling that of miliary tuberculosis. Histologic examination of an excised part of one of the tonsils revealed sarcoid of Boeck. Six months later the nodules of the iris and the pulmonary symptoms rapidly ameliorated. Spontaneous recovery occurred after three years.

WALLGREN, Göteborg, Sweden.

Diseases of the Eye

CESIUM IN THE MAMMALIAN RETINA. G. H. SCOTT and B. J. CANAGA JR., Proc. Soc. Exper. Biol. & Med. **40**:275 (Feb.) 1939.

In the course of routine spectrographic analysis of ox eyes for barium, cesium was found. Further analysis of both layers of the retina of 60 eyes from sheep, pigs and oxen by a quartz spectrograph revealed definite evidence of cesium. Examination of other tissue failed to reveal even traces of this element. It is a peculiar coincidence that an element so active photoelectrically is found only in a tissue layer which is capable of translating photon impacts into nerve impulses, but the authors make no attempt to attach any physiologic significance to the finding.

HANSEN, Minneapolis.

"SIMPLE UNCOMPLICATED" FORM OF CONGENITAL TOTAL COLOR BLINDNESS: REPORT OF A CASE. E. HEINSIUS, Klin. Monatsbl. f. Augenh. **101**:489 (Oct.) 1938.

A number of authors distinguish between "complicated" and "simple uncomplicated" congenital color blindness. The complicated form, presenting central amblyopia, photophobia, nystagmus and frequently changes in the macula, appears to be the most frequent. Heinsius reports the case of a youth aged 18 who had the simple uncomplicated form of congenital total color blindness unaccompanied by any other symptoms; his vision was perfect. The author concludes that this form is apparently rare and that its origin is probably to be found not in the retina but in a higher sensory center. Observation of the mode of heredity may furnish explanatory data.

K. L. STOLL. [ARCH. OPHTH.]

NONFAMILIAL JUVENILE DYSTROPHY OF THE CORNEA: REPORT OF A CASE. E. SAGHER, Klin. Monatsbl. f. Augenh. **101**:507 (Oct.) 1938.

Contrary to familial dystrophies of the cornea, the nonfamilial type is associated with somatic changes which point to developmental or degenerative disturbances. These are enumerated. They may involve the skull and the skeleton or manifest themselves as a tumor of the hypophysis or as lipoid degeneration of the brain or of the optic nerve.

Sagher reports the case of a girl aged 13 years, the youngest of four children, who had a corneal opacity at the age of 2. The cause was not known, but the girl was underdeveloped and underweight. Her skull and skeleton were normal, and the liver and spleen were normal in size and in function. Vision was reduced to 6/18 in the right and to 6/36 in the left eye; the intraocular tension was increased, and parenchymatous opacities existed without involvement of the epithelium or of Descemet's membrane. The fundus was normal and did not present any glaucomatous changes. The blindspot was of normal outline, and the field of vision showed a normal periphery. Treatment was of no avail. The corneal dis-

turbance resembled those accompanying gargoylism or dysostosis multiplex. The presence of choreatic twitchings corroborated the opinion that the corneal dystrophy was due to a developmental disturbance of a degenerative nature.

STOLL, Cincinnati. [ARCH. OPHTH.]

STEAM DOUCHE IN THE TREATMENT OF GONORRHEAL OPHTHALMIA. L. G. STEIGELMANN, Klin. Monatsbl. f. Augenh. **101**:572 (Oct.) 1938.

In gonorrheal conjunctivitis, injections of milk and of gonococcus vaccine may not produce a result before three to four days. To prevent sloughing of the cornea during these days, a douche is used which ejects steam at a temperature of 42 C. at a distance of from 10 to 15 cm. It is an apparatus consisting of a kind of thermos bottle connected with an atomizer. The steam is sprayed on the everted lids after the conjunctival sac is cleansed and after epinephrine hydrochloride is instilled. The author observed prompt disappearance of the swelling and decrease of the discharge within two to three days. Analgesic and sedative preparations are added to the steam-forming solution. STOLL, Cincinnati. [ARCH. OPHTH.]

Skin Diseases; Allergy

NONTUBERCULOUS ERYTHEMA NODOSUM. J. SURANYO, Arch. Pediat. **56**:1 (Jan.) 1939.

A boy of 6 years presented erythema nodosum following an attack of cervical adenitis on two occasions. Tuberulin in strong dilutions failed to produce a positive reaction.

NICOTINIC ACID IN THE TREATMENT OF ACRODYNIA. FREDERICK F. TISDALL, T. G. H. DRAKE and ALAN BROWN, J. Pediat. **13**:891 (Dec.) 1938.

Six infants ranging in age from 8 months to 2 years, suffering from acrodynia, were treated with nicotinic acid. Two forms of the drug were used, pure nicotinic acid and the monoethanolamine salt of nicotinic acid. No difference was found in the action of these two substances. The drug was administered parenterally in order to obviate any possibility of defective absorption from the intestinal tract. The first dose (20 mg.) was given intravenously, and subsequent doses of from 20 to 40 mg. were given intramuscularly twice daily. The only reaction noted was redness and blotching of the skin in 2 babies, occurring shortly after the injection and lasting only one-half hour. In a few cases the drug was given by mouth, 100 mg. a day being given to the younger and 125 mg. a day to the older infants. In addition, all the infants were given a diet consisting of milk, egg yolk, a mixture of equal parts of pablum, wheat germ, and a finely ground green oat grass very rich in the vitamin B complex, oleum percomorphum, orange juice and in the cases of the older infants, liver. Nicotinic acid seemed to hasten the healing of the cutaneous lesions, but no evidence was found that it shortened the period of recovery from the disease.

RAUH, Cincinnati.

ACRODYNIA TREATED WITH INTRAMUSCULAR INJECTIONS OF VITAMIN B_1. JAY I. DURAND, V. W. SPICKARD and ERNEST BURGESS, J. Pediat. **14**:74 (Jan.) 1939.

Two cases of acrodynia treated with intramuscular injections of vitamin B_1 are described. Three days after the treatment was begun, marked improvement occurred. In both cases the improvement ceased, and the symptoms grew worse when the injections were discontinued and the vitamin was given by mouth. In

spite of the relapses which recurred when treatment by mouth was given, both patients recovered in six weeks from the beginning of injection treatment.

RAUH, Cincinnati.

THE LEUKOPENIC INDEX IN PEDIATRIC ALLERGY. PAUL HOGG, Virginia M. Monthly **66**:108 (Feb.) 1939.

From a study of the leukopenic index in a short series of cases in which clinical symptoms suggesting allergy were present but in which cutaneous reactions were negative, it is concluded that the leukopenic response to milk, egg and wheat is of diagnostic value in the study of allergy in any infant or child.

STONE, Richmond, Va.

TWO CASES OF ANAPHYLACTOID (HENOCH-SCHÖNLEIN) PURPURA. DONALD BATEMAN, Proc. Roy. Soc. Med. **32**:327 (Feb.) 1939.

The cases of 2 children, aged 5 years and 4 years respectively, are reported. Both complained of severe colic, abdominal pains of many days' duration and a purpuric rash. The family history, past history, onset of symptoms, results of investigations and full progress notes during the stay in the hospital are given in the reports.

WILLIAMSON, New Orleans.

CONGENITAL TROPHEDEMA WITH MULTIPLE LOCALIZATIONS. A. SÉZARY and P. GRENET, Bull. Soc. franç. de dermat. et syph. **46**:49 (Jan.) 1939.

The authors describe a case of congenital trophedema in a 14 month old boy. The condition was neither hereditary nor familial. It was considered unusual on account of the involvement of both upper extremities and the left half of the face. The child was healthy. The disease was considered a type of nevus.

LAYMON, Minneapolis. [ARCH. DERMAT. & SYPH.]

INFANTILE ASTHMA AND ECZEMA, J. COMBY, Bull. Soc. pédiat. de Paris **36**:438 (July) 1938.

Asthma is viewed, in agreement with Trousseau's description, as a paroxysmal respiratory neurosis. Comby regards it as hereditary. The families of many asthmatic children exhibit conditions similar to asthma, while those of other such children have histories of conditions such as migraine, gout, diabetes, obesity, gravel and neuroses, which Comby calls dissimilar hereditary conditions related to asthma. They are among the manifestations of the arthritic diathesis, as are asthma and eczema. The author does not subscribe to the tenet that the earlier in life the asthmatic attacks begin, the sooner they are likely to disappear. He believes that in most truly asthmatic persons of advanced age the condition is carried over from youth, even though its manifestations may have been mild for a long time. He does not think real cures are obtained with treatment any more than they are in gout and diabetes. Epinephrine and ephedrine are valuable in the treatment of actual crises.

BENJAMIN, Montreal, Canada.

ENORMOUS PIGMENTED AND VERRUCOUS NEVUS. V. HEIMANN, Bull. Soc. pédiat. de Paris **36**:636 (Nov.) 1938.

A boy 8 years old had a great many pigmented nevi on the face, arms and back and covering the entire left thigh. There were verrucous projections in some, as well as hair. No treatment was instituted, but it was intended to keep him under observation from time to time to detect any changes that might occur. It is stated that malignant degeneration occurs less frequently in the verrucous than in the flat type of pigmental mole.

BENJAMIN, Montreal, Canada.

ASTHMA FOLLOWING ECZEMA IN THE CHILD. P. MAYNADIER, Bull. Soc. pédiat. de Paris **36**:707 (Nov.) 1938.

A girl who had had eczema at the age of 2 months began to show manifestations of severe asthma when 3½ years old. When asthmatic seizures disappeared for a time, eczema became more marked and vice versa.

BENJAMIN, Montreal, Canada.

ERYTHEMA NODOSUM. R. DEBRÉ, A. SAENZ, R. BROCA and R. MALLET, Rev. franç. de pédiat. **14**:433, 1938.

The authors devote sixty pages to their discussion of erythema nodosum. They believe that the lesions are not allergic but due to the actual presence of tubercle bacilli as a result of a transient bacteremia, occurring usually coincidentally with the development of a primary pulmonary lesion. They have recovered organisms from the nodules in 2 cases, from the blood in 5 and from stomach washings in 16, of a total of 35 cases studied. In a case in which tubercle bacilli were found in the nodule, the tuberculin test became positive only after a seven month interval. During this time the child was not in contact with any tuberculous person.

LESLIE, Evanston, Ill.

INFANTILE POIKILODERMA. W. JECKLI, Monatschr. f. Kinderh. **78**:73 (March) 1939.

A 2½ year old baby presented diffuse pigmentation and atrophy of the skin, total disappearance of all hair, including the lanugo, recessive changes in the nails, microdontia, bilateral cataracts and dwarfism.

GERSTLEY, Chicago.

Surgery and Orthopedics

EFFECT ON WOUND HEALING OF BACTERICIDAL ULTRAVIOLET RADIATION FROM A SPECIAL UNIT. D. HART and P. W. SANGER, Arch. Surg. **38**:797 (May) 1939.

Experimental wounds were exposed to bactericidal radiation. Such wounds healed somewhat better than control wounds. Exposure of the peritoneum to this intensity of radiation produced no damage demonstrable by adhesions, edema or increased fluid in the cavity. The authors concluded that bactericidal irradiation which will render the air in the operative region almost free of viable organisms offers little, if any, risk of damage to the patient. It was noted that healing is better in an irradiated wound than in one not irradiated, there being less danger of infection and less local systemic reaction.

KAISER, Rochester, N. Y.

FRACTURES OF THE MORPHOLOGICAL NECK OF THE HUMERUS IN CHILDREN. L. J. AUSTEN, Canad. M. A. J. **40**:546 (June) 1939.

Four cases of fracture of the morphologic neck of the humerus are presented. This fracture is not common and is often described as an epiphysial separation of the upper epiphysis of the humerus. The line of separation is seldom true, however, as part of the inner side of the shaft is usually carried away with the epiphysis.

Open reduction is needed in most cases.

MOORE, Omaha.

FRACTURES OF THE RADIUS OR ULNA—LOWER FIFTH—IN ADOLESCENCE. DONALD E. MCKENNA, New York State J. Med. **39**:692 (April 1) 1939.

The most frequent site of fracture of both bones of the forearm in childhood and adolescence is in the lower fifth. The distal radial fragment is usually displaced posteriorly, producing a deformity similar to that of Colles' fracture. The

treatment differs from that of Colles' fracture, and reduction is best obtained with the patient under general anesthesia. McKenna feels that open reduction is indicated if satisfactory results are not obtained by manipulation, because minor degrees of malposition produce considerable disability.

AIKMAN, Rochester, N. Y.

APHASIA AND AMNESIA FOLLOWING FRACTURE OF THE SKULL. DEGIRARDIER, Bull. Soc. pédiat. de Paris **36**:733 (Dec.) 1938.

A girl 7 years old had aphasia, alexia and agraphia three days after injury to the head. There was a fracture of the posterior part of the left temporal bone, which was depressed beneath the edge of the parietal bone. At operation the depressed bone was lifted and considerable subdural clot was washed out through a tear in the dura, which was enlarged. The subjacent brain was contused, and some fragments of contused brain tissue came away with the blood clot. The girl recovered. When last seen, twenty-two months later, she was perfectly well.

BENJAMIN, Montreal, Canada.

FOUR ELECTRIC BURNS IN CHILDREN: TREATMENT BY PLASTIC SURGICAL MEASURES. H. LEMPKE, Deutsche Ztschr. f. Chir. **251**:331 (Dec.) 1938.

The operative repair of burns received by 4 children who inserted electric outlets (220 volts, alternating current) into the mouth is described. One child, aged 18 months, remained feverish and semicomatose for five days after the shock. Lumbar punctures to lower the elevated spinal fluid pressure were beneficial. Recovery was complete.

HARRIS, Durham, N. C.

CONGENITAL CLUBFOOT. K. GAUGELE, Med. Klin. **35**:310 (March 10) 1939.

The author advocates treatment beginning as early as the seventh or eighth day of life. He describes and illustrates the application of adhesive tape according to the method of Spitzy. Experience is necessary for correct application, especially as regards tightness of the bandage. Interference with circulation must be avoided carefully, and at first the nurse should observe the toes every half hour. The first three weeks' treatment should be carried out in the hospital. As a rule the feet are normal after six or eight weeks. After the bandage is omitted, braces are worn and the feet are exercised. At times braces are alternated with bandages. As soon as the child begins to walk, orthopedic shoes are worn. In general, results are excellent. In late cases operation may be necessary. The author discusses his method, which allegedly yields excellent results.

SIEMSEN, Chicago.

TREATMENT OF BURNS—WITH SPECIAL REFERENCE TO THE USE OF SOLUTIONS OF SILVER NITRATE, ANILINE DYES AND THEIR COMBINATION. C. Y. CHEN, Chinese M. J. **55**:407 (May) 1939.

The wound is cleansed with a boric acid solution, and any oil or grease is removed with soap and water, This is followed by spraying with a 1 per cent aqueous solution of gentian violet, and ten minutes later by painting with a 10 per cent solution of silver nitrate. Thereafter, at fifteen minute intervals, the burned surface is sprayed two or three times with the solution of gentian violet.

All burns are studied bacteriologically. When they are found to be infected with gram-negative organisms, they are treated with a solution made of equal parts of gentian violet, acriflavine and brilliant green. Chen reports good results in a series of patients, the majority of whom were children. He uses protective measures against dehydration and loss of proteins.

NEFF, Kansas City, Mo.

Teeth and Dentistry

EFFECTS OF SELECTIVE SALIVARY GLAND EXTIRPATION UPON EXPERIMENTAL DENTAL CARIES IN THE RAT. V. D. CHEYNE, Proc. Soc. Exper. Biol. & Med. **42**:587 (Nov.) 1939.

Eighty-eight rats 22 days of age were placed on two different diets, one known to be productive of caries and the other the regular stock diet found to produce little change in the teeth. From groups of rats in each series various salivary glands were extracted. It was found that this disturbance of the normal salivary flow resulted in an increase in the incidence of caries. HANSEN, Minneapolis.

DENTAL CARIES AND NUTRITION: INVESTIGATION OF CHILDREN FROM NORWEGIAN ELEMENTARY SCHOOLS AND INFANT HOMES. E. H. SCHIOTZ, Brit. Dent. J. **66**:57, 1939. DENTAL CARIES AND NUTRITION, Nord. hyg. tidskr. **19**:242, 1938.

DESTRUCTION OF TOOTH ENAMEL BY ACIDIFIED CANDIES. E. S. WEST and F. R. JUDY, J. Dent. Research **17**:499 (Dec.) 1938.

INFANTILE MELANODONTIA. G. BELTRAMI and M. ROMIEU, Rev. de stomatol. **41**:433 (June) 1939.

The authors report studies on lesions which have previously been confused with dental caries. These lesions are described as disintegration of dental tissues and deposition of melanotic pigment; there may be pulpal involvement. The lesions have no effect on the permanent teeth, are almost entirely confined to the maxillary deciduous incisors and differ both clinically and anatomically from caries in their onset, form and evolution. The authors believe the etiology involves a nutritional disequilibrium resulting from modern diets.

NEWCOMB, Cleveland. [ANGLE ORTHODONTIST.]

DIATHERMY IN DENTISTRY. S. GARBARSKA-SARCINA, Brit. J. Phys. Med. **2**:130 (May) 1939.

A new stimulus has been given to the treatment of the roots of teeth by the introduction of diathermy into dentistry. Both forms of diathermy, medical and surgical, are employed. The medical type is used for postoperative pain and for all inflammatory processes of the jaw. Recently, short wave radiation has been employed for the same purpose.

Roentgenograms are presented which show the results obtained one and two years after devitalization of the pulp by diathermy, followed by subsequent filling of the root canal. They show neither apical foci nor any abnormal changes. Other roentgenograms are presented which show the results of the treatment of already existing focal infections. HARTMAN, Cleveland.

STUDIES OF DENTAL CARIES. I. JUNDELL, Acta pædiat. **24**:428, 1939. CLINICAL INVESTIGATIONS OF THE GENESIS AND PREVENTION OF DENTAL CARIES. I. JUNDELL and J. BILLING, ibid. **23**:293, 1939.

Jundell reports on the disappointingly negative results of a ten year study of the prophylaxis of dental caries, echoes of which have been heard from time to time in *Acta paediatrica*.

Commencing in the spring of 1926, steps were taken to assemble two large groups of children, a control group and a study group. The members of the control group were followed without administering special treatment; this group numbered 113 children. The members of the study group consisted of children

whose mothers had been given vitamin D during the last ten weeks of pregnancy and who themselves had received ample amounts of vitamin D and a good diet until the end of the second year of life. The group numbered 135 children. At 2 years of age they were separated into two smaller groups, the first consisting of 57 children who received no special treatment thenceforward, and the second consisting of 78 children, who continued to receive vitamin D periodically through the winter months. Although the members of both the treated and the control groups lived in their own homes, they were carefully supervised by a trained personnel of visiting nurses, and all received a good diet. Little dental treatment was accorded to any of them until they commenced to attend school; thenceforth cavities were promptly filled by the school dentists.

Periodic examinations of the state of the teeth were made by those engaged in the study at regular intervals until the children were between 7½ and 8½ years old.

Succinctly, these examinations revealed clearly and unequivocally that the incidence of caries of both the deciduous and the permanent teeth was not in the least diminished by the measures that had been taken. McCUNE, New York.

Miscellaneous

OBSERVATIONS UPON THE EXPERIMENTAL USE OF SULFAPYRIDINE: I. THE RELATION OF STRAIN RESISTANCE TO THE CHEMOTHERAPEUTIC EFFECTS OF SULFAPYRIDINE IN EXPERIMENTAL PNEUMOCOCCAL INFECTIONS IN MICE. P. H. LONG and E. A. BLISS, Ann. Int. Med. **13**:232 (Aug.) 1939.

The conclusions reached by the authors indicate that marked differences exist among strains of pneumococci in their response to the chemotherapeutic effects of sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine).

READING, Galveston, Texas.

TOXIC MANIFESTATIONS IN THE SKIN FOLLOWING SULFANILAMIDE THERAPY. J. W. TEDDER, Arch. Dermat. & Syph. **39**:217 (Feb.) 1939.

Tedder concludes that sulfanilamide therapy may result in several distinct types of toxic dermatosis. The first and most common type is precipitated by exposure to sunlight. In this type the level of sulfanilamide in the blood is not abnormally high, nor is there ordinarily any sensitivity to the drug. However, the combination of factors occurring internally, such as a possible abnormality in porphyrin metabolism, a decrease of resistance due to the disease and the irritative effects of the sun's rays, results in the occurrence of localized dermatitis, which may be complicated by dermatitis at distant points. The second type of eruption is that in which definite sensitivity to the drug occurs, resulting in sensitization dermatitis. The patient cannot tolerate further sulfanilamide in any dose. The third type of dermatitis is that resulting from poor toleration of, or saturation with, sulfanilamide and presenting the typical picture of toxic dermatosis. The toxic effects of the drug result from improper utilization of the drug or from its gradual accumulation in the system. The patient can tolerate further sulfanilamide therapy provided excretory functions are normally resumed and the dosage is properly modified. There is no known sensitivity to the drug in these cases.

JACKSON, Iowa City.

PATHOLOGIC CHANGES IN RATS AND DOGS FED DIETS CONTAINING LEAD AND ARSENIC COMPOUNDS. L. L. FINNER and H. O. CALVERY, Arch. Path. **27**:433 (March) 1939.

The ill effects of lead arsenate, arsenic trioxide, calcium arsenate and lead acetate on rats and dogs are reported. (The study has not been completed because

of withdrawal of support by an act of Congress). Litter mates fed with an adequate diet were used. The quantities of arsenic and lead given, the methods of histologic examination and the special technic of the examination of lead-treated animals are described.

Rats that had received 500 Gm. of a diet containing 2.65 mg. of lead acetate per gram showed dulness of hair, moderate secondary anemia, basophilic stippling of red cells and large deposits of iron in the spleen. Enormous quantities of lead were found in the bones and cartilages; large quantities were demonstrated in the kidneys, but none in other organs. There was marked irregularity of the tubular epithelium of the kidneys, with hypertrophy of the nuclei of many epithelial cells and eosinophilic inclusion bodies in the nuclei and also in the cytoplasm. Animals that had received large quantities of arsenic trioxide showed generalized dilatation of capillaries in the viscera and parenchymatous degeneration of the liver.

The conclusion reached is that the ingestion of lead and arsenic gives rise to chronic tissue poisoning and that continued intake of these metals into the body is always fraught with the danger of definite injury. APFELBACH, Chicago.

NEW MILK BOTTLE—A MEANS OF LESSENING THE SPREAD OF COMMUNICABLE DISEASES. J. M. SANSBY, Arch. Pediat. **56**:650 (Oct.) 1939.

Evidence is presented that the bottle described and illustrated is ideal for preventing contamination of milk by way of the bottle lip. ORR, Buffalo.

GRANULOCYTOPENIA CAUSED BY SULFAPYRIDINE IN CHILDREN. N. ROSENTHAL and P. VOGEL, J. A. M. A. **113**:584 (Aug. 12) 1939.

Treatment with sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine), given intermittently or for relatively long periods, was followed in 3 children by granulocytopenia. Two of the patients died; they had shown no return of marrow function in examinations of the blood or of the bone marrow.

Granulocytopenia and jaundice are the two most severe toxic effects that this drug produces. Jaundice usually occurs early, but leukopenia may be late and should be watched for by examination of the blood and sternal marrow.

HEERSMA, Kalamazoo, Mich.

RELATION OF CONCENTRATIONS OF FREE TO CONJUGATED SULFAPYRIDINE IN THE BLOOD OF PATIENTS. A. T. WILSON, D. KAELY and G. E. CULLEN, Proc. Soc. Exper. Biol. & Med. **42**:187 (Oct.) 1939.

In a study of 26 children given standard doses of sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) 100 determinations were made of free and total sulfapyridine in the blood at various intervals. It was found that wide variations occurred in the values of free and total sulfapyridine, whereas the conjugated form (acetylsulfapyridine) in most cases was present to the extent of almost 2 to 3 mg. per hundred cubic centimeters of blood. HANSEN, Minneapolis.

INVESTIGATION INTO THE PHOTO-DYNAMIC ACTION OF SULPHANILAMIDE COMPOUNDS. A. EIDINOW, Brit. J. Phys. Med. **2**:150 (June) 1939.

On the basis of both clinical observation and laboratory experiments, Eidinow comes to the conclusion that ultraviolet radiation may be safely applied locally and generally in combination with drugs of the sulfanilamide group.

HARTMAN, Cleveland.

Miscellaneous

LATE RESULTS OF TREATMENT AT BOURBOULE OF CHILDREN HOSPITALIZED IN THE THERMAL HOUSE: TRACHEOBRONCHIAL ADENOPATHIES, REPEATED BRONCHITIS AND OTHER CONDITIONS SUITABLE FOR TREATMENT. J. HALLÉ and P. FERREYROLLES, Bull. Soc. pédiat. de Paris **36**:444 (July) 1938.

Few children did not benefit from a stay at this institution for convalescents. The younger ones did as well as the older ones. Improvement in the conditions for which the children were sent to the thermal house was noted, although it usually took some time. The results were good in children with asthma, bronchial dilatation after pneumonia, recurrent bronchitis and tracheobronchial adenopathy, especially that secondary to whooping cough and measles.

BENJAMIN, Montreal, Canada.

INVESTIGATIONS COMPARING ARTIFICIAL WOOL MATERIALS WITH COTTON MATERIALS. E. WOLTERS, Arch. f. Hyg. **121**:1 (Oct.) 1938.

Wolters investigates the hygienic properties of so-called cellwool, an artificial wool made from different kinds of cellulose and used by the clothing industry. He compared pure cotton materials and cotton materials with from 16 to 70 per cent of cellwool with pure cellwool materials.

Pure cellwool materials and those of cotton mixed with a high percentage of cellwool showed a greater retention of water than pure cotton materials. The source of the cotton and the volume of the pores of the materials influenced the amount retained. Similarly, pure cellwool fibers and the high cellwool mixtures absorb water more readily than the fibers of pure cotton materials or of materials having a low content of artificial wool; the same is true for their power of absorbing water. Permeability to air differed very little between cellwool and cotton materials.

Wolters considers these materials to be of equal value from a hygienic standpoint.

FALKENHEIM, Rochester, N. Y.

EARTHEN FEEDING VESSELS OF THE BRONZE AGE FOUND IN HUNGARY. J. V. BOKAY, Jahrb. f. Kinderh. **148**:226 (Jan.) 1937.

Descriptions and illustrations of several types of feeding vessels are given. Some are badly damaged, but others are in a comparatively good state of preservation.

LANDAU, Hannibal, Mo.

A MODEL SCHEME FOR A DEPARTMENT FOR CHILDREN AT A CENTRAL HOSPITAL. A. LICHTENSTEIN, Acta pædiat. **24**:457, 1939.

This paper presents the report made by the executive committee of the Swedish Union of Pediatricians concerning the architectural features of a model pediatric division of a large general hospital. The physical requirements of such a unit are discussed, and drawings of plans are submitted.

MCCUNE, New York.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

GERARD KROST, M.D., *President, in the Chair*

Regular Meeting, Feb. 20, 1940

The Community Deals with the Juvenile Delinquent. MISS IRENE KAWIN, Deputy Chief Probation Officer, Juvenile Court of Cook County.

During the year 1939, the juvenile court of Cook County considered more than 1,500 new cases of juvenile delinquency, more than 300 new cases of truancy and more than 150 new cases of feeblemindedness. A large percentage of the feebleminded children have been delinquent children who have been referred by the Court to the Institute of Juvenile Research and are found to be subnormal. The present facilities for taking care of these groups are inadequate. The following recommendations are advanced:

An adequate adjustment service should be a part of every school. Deviates in scholarship or conduct should be given thorough case work service. Removal of a child from his home should be based on the total situation, and the type of placement should be determined by the needs of the child. This would require funds for boarding in private homes, as well as more varied institutional service. Institutions for dependent children should admit children who present problems.

Within the crime prevention bureau of the police department there should be a small social service staff to modify the methods of the police in handling juveniles.

The juvenile court should be so organized that it can deal adequately with the serious cases which must be handled there. Hearings should be few and almost private. Officers should have time to do a thorough case work job on every case.

The juvenile detention home should be a place for study and adjustment of the child.

Reformatories should be equipped to give the children committed to their care the highest type of individualized treatment: vocational, educational, physical and mental.

The Community Deals with the Juvenile Delinquent. MR. CHESTER SCOTT, District Probation Officer, Juvenile Court of Cook County.

In 1939 the Chicago police department reported a total of 11,549 investigations of complaints against juveniles; of this number, 10,007 were of such minor nature that they were adjusted without court action. The remaining 1,542 complaints were brought to the attention of the juvenile court by filing delinquent petitions.

This group was disposed of by the court as follows: probation of guardianship, 1,158; committments, 335; continued generally, 25; dismissed, 23.

The juvenile court carries on a sorting procedure whereby boys are given the opportunity to work out their own adjustment in society if they are able to do so, the force of authority being reserved for such children as are not susceptible to socializing processes. Trained probation officers have the ability to analyze and sympathize with the boy's problems and to bring about the best cooperation from the offender and from the community. The real process of adjustment, however, can be effected only indirectly through pressure applied by society as a whole.

Only a small percentage of boys get into trouble; and if this percentage were evenly distributed throughout the population, control would be a more simple problem. In some neighborhoods, however, usually slums, the number of delinquents

is so great that delinquency becomes the accepted pattern of behavior. Neighborhoods as well as personalities must therefore be evaluated. Boys in certain neighborhoods tend to indulge in a certain type of offense, to the exclusion of other forms of crime. Special problems are thus involved, because the offense tends to become a sport in which the boys seek to outdo one another.

The solution of the problem must be laid on the community. Whether the motive for wanting to control others is a desire for self protection or a sympathetic desire to help, the things one wishes to do for other people cannt be forced on them, even by those in possession of great authority. An effective control must be established before the problem becomes formalized to the extent that it is brought under the jurisdiction of the courts.

DISCUSSION

DR. G. F. MUNNS: Mr. Scott and Miss Kawin have indicated pretty clearly that the state of Illinois has a great deal to do in order to take care of delinquent children properly, and they have also indicated clearly that an important phase is preventive work. That type of work lies clearly in the sphere of influence of this society. I believe the pediatrician can have much to do with the care of juvenile delinquents—not so much by contact with the juvenile delinquents themselves but in fostering preventive methods in the home and particularly in the schools. It seems to me that a school system has an important function to perform in this respect. The people of the nation have to spend, and are willing to spend, millions of dollars on penal institutions when, with a fraction of this sum, they could prevent a number of these problems. I hope that from now on the Chicago Pediatric Society and all physicians who have any interest in the welfare of the community will have a real and active interest in the problems of juvenile delinquency.

You spoke of boarding homes. What are your standards for boarding homes, and where do you choose them—in the neighborhood or in the country, nearby or far away?

DR. MAURICE L. BLATT: We members of the society should be grateful to Mr. Scott and Miss Kawin for bringing this problem before us, and presenting their analysis of a situation that does, as they say, influence the community as a whole. It would seem that the problem is not entirely a medical one. The problem of delinquents is to a large degree one of environment; in part it is the result of a change of environment whereby people from farms and smaller communities are brought into our community, inadequately housed, badly provided for and given comparatively little remunerative work. It is a community responsibility rather than a medical one. As an example, a great proportion of the Negro population was brought here by the stockyards and the railroads a number of years ago, when labor was badly needed. These people were not provided for economically, and no responsibility was placed on the organizations who "sold" them the idea of coming here.

Were that constant in all communities, it would not be so significant. It is not constant, however, and in other communities industries take responsibility for their employees. In Honolulu, where laborers are of a like or lower stage of intelligence, such people are well cared for medically and economically. In Chicago the problem should be one of industrial responsibility, not a medical problem. The medical problem should be concerned with the constitutionally psychopathic persons, weeding them out and placing them in environments where they can do no harm. That problem should be ours as pediatricians. Civic or industrial agencies should take care of the housing problem.

We have had a committee for a number of years, composed of Drs. Kraft, Beverly and Levinson, working for replacement of these psychopaths. I do not know what proportion of delinquency is on account of environment or what proportion is due to constitutional inferiority, but I should like Mr. Scott to give us his idea of what proportion falls in each category.

DR. C. A. ALDRICH: I was interested to hear Miss Kawin say the delinquent children did not come from happy homes. After all, pediatricians in their work with

families have a good deal to do with making home conditions satisfactory, and so it is possible that we could do some good in lessening the delinquent problem among children.

DR. H. E. IRISH: In connection with your statements about happy homes, is it possible that some of these delinquents come from families in which all are happy in their delinquency? I might say that I have labored in forgotten neighborhoods, in my association with Emerson Settlement House, and I can recall delinquent families who lived on what they could purloin. The whole family had an utter disregard for property rights. This was a variety of delinquency, and yet in the same family a rigid sexual morality was maintained. The girls were strictly supervised. I can recall another neighborhood where the entire community thrived on the coal thrown at them by brakemen or on that thrown by the little boys who were pushed over the railroad fence for the purpose of throwing over coal.

MISS IRENE KAWIN: The police officer for juveniles is chosen from the police force. He does not wear a uniform. There is nothing done to train him, but in working with us for a time he gets our point of view. When Judge Barthelme was judge of the court, all these men were interviewed by her and she passed on them. I think if there were a small staff of social workers within the police department they could work out the problem, station by station. The procedure is at present a little haphazard, but if there were a small staff of social workers in the station, they would develop a uniform technic. The police have no means of ascertaining which cases might be settled and which must come into court.

Studies have been made which show that the members of the criminal population and juvenile delinquent population are about the same as the average nondelinquents in the community, and the feebleminded are about the same. Many feebleminded people are adjusted satisfactorily in the community and it is not known they are feebleminded. We feel the percentage of feebleminded persons is about 10 per cent of the population. We discover the condition when they become delinquent; we think it is their personalities which are at fault, and we have them studied. The only time the general population is studied is during war, when persons are examined for the army. We have inadequate facilities for caring for these people. The institutions are always crowded, and we have a commitment law based on the assumption that the child will spend his life in the institution. We should have a more adjustable program. Many of these children can be rehabilitated.

The county appropriates $4,000 a year to be administered under child-placing agencies for dependent children who are not delinquents. We have a small fund, $7,000 a year, which we administer directly, that is, for temporary placement. We have to place about 10 to 14 children a day about whom we know nothing. The homes are practically all within the city limits, because the children have to be placed quickly. The child-placing agencies use homes in the outlying districts, not too far away for the parents to visit. The state requires that no child be placed in a home where the family depends on the board of the child.

I think it is true that back of the child delinquent there is always a certain tension in the home, something that is inadequate. The delinquency does not start until the child gets out on the street; while he is in his home his mistakes are pretty well taken care of. I do not think delinquent children will be found in homes where the parents are happy and easy-going.

Book Reviews

Die Pädiatrie Meiner Zeit. By Adalbert Czerny. Price, 6.60 marks. Pp. 124, wth no illustrations. Berlin: Julius Springer, 1939.

Dr. Adalbert Czerny's medical career covers almost completely the development of scientific pediatrics; thus it represents an interesting historical summary of German pediatrics during this period. It is to be noted that Czerny spent several years actively working in the medical sciences which he regarded as essential to the training of the specialist who is to contribute to development of pediatrics. The breaking away from internal medicine by way of medical care of the infant and gradual development of independent clinics in the universities is of great interest.

In his early years, when he was an assistant, the care of children was usually left to the youngest and most inexperienced assistant. No histories were taken, and the treatment was schematized. In the outpatient clinic the care of the patient left everything to be desired. In 1894 no German medical student was required to take work in pediatrics. When Czerny was called to Breslau he said he would come if the following conditions were fulfilled: 1. A clinic supported by the state and of equal rank with the other clinics should be established. 2. There should be obligatory pediatric training for all students. 3. There should be examinations in pediatrics. In Czerny's newly established clinic at Breslau, the outpatient clinic was made an important cog in the machinery; it was open all day. As the ideal for a pediatric clinic he postulated a division for infants, a division for older children, a department for infectious diseases and an outpatient department. In addition he demanded a pavilion for tuberculosis and a clinic for mental diseases and for mental hygiene.

One of the most important changes in feeding of infants was the restriction to five meals from the very start. It was recognized that the composition of the food was of rather greater importance than various methods of its sterilization. It is rather difficult to subscribe to the apodeictic statement that the maximum daily milk allowance during infancy is 500 cc.

At the time Czerny began work, the French journals were the leading pediatric periodicals. These were read in order that the latest developments in pediatrics might be learned. The only German pediatric periodical was the *Jahrbuch*. Forty years later there were six journals of pediatrics. I miss mention of one of the most outstanding German books on pediatrics, "Des Kindes Ernährung und Ernährungsstörungen," by Czerny and Keller.

The constitutional differences in children was one of Czerny's special hobbies. The clinical entity of the exudative diathesis is known to most pediatricians.

The Kaiserin August Victorin Haus was evidently not to Czerny's liking, as he describes it in these words: ". . . externally a palace, internally a poorly built infants' home, in which was demonstrated how by spending large sums of money one could keep a few infants alive." In the chapter devoted to feeding, the author runs the gamut of the various sugars and the therapeutic foods, such as buttermilk and malt soup. Many would differ with his opinion that Finkelstein's *Eiweissmilch* (albumin milk) is of no greater value than modified buttermilk.

Czerny lived through the entire period of discovery of tuberculin, its use in therapy and finally its relegation to diagnostic use. He cites two interesting results of the enforced fat-free diet during the World War: the disappearance of scarlet fever and the tremendous increase in tuberculosis among children. The most thrilling and significant event in his medical life he considers to have been the introduction and use of diphtheria antitoxin. Only those who saw diphtheria in preantitoxin days can appreciate this.

Czerny closes by saying, "My time is up and now the younger men must carry on."

Die übertragbare Kinderlähmung mit besonderer Berücksichtigung der Erfahrungen aus der Kölner Epidemie 1938. Edited by Prof. Dr. Hans Kleinschmidt. Price, cloth, 17.80 marks; paper, 16 marks. Pp. 339, with 26 illustrations. Leipzig: S. Hirzel, 1939.

This volume describes an epidemic of infantile paralysis which occurred in Cologne during 1938. It covers etiology, epidemiology, pathologic anatomy, constitutional heredity and predisposing factors; it gives statistics on preparalytic, abortive and paralytic types of the disease and outlines the orthopedic methods of treatment and prophylaxis. Each subject was considered by a specialist in that field. There were 476 cases, in 38 (7.9 per cent) of which the patients died. The patients in 249 cases were cured with but little residual paresis; 131 patients were improved, and 58 were completely cured. In general, the observations were similar to those known to most American physicians. A few conclusions were interesting. The authors feel that more stress should be placed on blood groupings, believing as they do that persons with blood of some groups have a constitutional predisposition to the disease.

The authors subscribed to the general view that the virus enters the human economy by way of the nose, although they did not deny the possibility of the gastrointestinal tract as a portal of entry. Twins were studied to rule out the influence of heredity. They observed that at least one third of the persons exposed showed pathologic evidence in the spinal fluid with or without symptoms. They felt that the virus was not only neurotropic but lymphotropic. It was stated that such factors as physical strain, wetness and cold predisposed a person toward infection. They thought that poliomyelitis might be diagnosed or at least suspected in any person if there was fever or pain when the muscles were extended or pressed and if these symptoms were accompanied by some hyperesthesia and perhaps meningismus, even without paresis or paralysis. In their experience, the first specimen of spinal fluid was often entirely normal, while the second one, obtained a short time later, would show a high degree of pleocytosis.

The seventh nerve was the cranial nerve most commonly involved in this series. In 29 cases (9.4 per cent) it was the only nerve involved. (They ruled out rheumatic infection of the seventh nerve by denying its existence.)

The efficacy of convalescent serum was questioned, but it was stated that its use could not be discarded entirely and that probably some future experimentation will show why it does not give better results. It was also felt that more work should be done with an animal serum. They mentioned the fact that in monkeys and certain bovine species the disease has developed spontaneously.

Artificial fever treatment was tried with no effect. They extolled the effect of active and passive motion, which they considered more important than massage.

Communicable Diseases for Nurses. By A. G. Bower, M.D., and E. B. Pilant, R.N. Fourth edition. Price $3. Pp. 550, with 73 illustrations. Philadelphia: W. B. Saunders Company, 1939.

This book has been enlarged by the addition of chapters on gonorrhea, syphilis, tuberculosis and poliomyelitis as well as by instructive chapters on public health control of communicable diseases, subjects at present receiving widespread attention.

The careful definition of terms should prove useful to teacher and pupil.

Aseptic technic is well treated in the illustrations and chapters on gown technic, hand scrubbing, barrier and unit setup and other procedures. This should be especially helpful to the teacher, the public health and the private duty nurse and the mother taking care of the patient in the home without nursing help.

Chapter V, on public health control of communicable diseases, covers problems encountered in the prevention of the spread of these disorders.

As in previous editions, the various diseases are adequately described. Colored and black and white illustrations of rashes and other diagnostic symptoms, such as the swelling of mumps and Koplik's spots of measles, are splendid. The chap-

ters on tuberculosis are necessarily extensive, as few nurses become familiar with this disease during their student days. Poliomyelitis also receives a great proportion of space.

To the nurse who did not have special training in communicable diseases this book should prove helpful as a handy reference in either private duty or public health work. To the educator specializing in teaching communicable diseases, it may offer useful suggestions.

The glossary deserves special praise for its completeness.

Handbook of Public Health Bacteriology and Chemistry. Edited by M. S. Marshall, Department of Public Health, City and County of San Francisco, California. Second edition. Price, $1.50. Pp. 150, with no illustrations. San Francisco: J. W. Stacey, Inc., 1939.

This is the second edition of a manual which was received with enthusiasm by laboratory workers when it first appeared in 1937. The book fills the need of technicians for a brief outline of laboratory procedures essential in public health and hospital work. The laboratory procedures to be followed in connection with the control of communicable diseases are especially well described. Inclusion of formulas for special bacteriologic culture mediums is a feature which rounds out the handbook and is a valuable time saver. The second edition is more complete than the first and includes recent developments in public health laboratory technic.

The book is of more value to technicians in small laboratories, where they are required to carry out a wide variety of work, than to those in large laboratories, where they are assigned to specialized procedures. The directions are concisely written, and the handy pocket size of the publication makes it particularly convenient for rapid reference. The second edition should be welcomed by laboratory workers throughout the country.

Treatment of Some Common Diseases (Medical and Surgical). By various authors, edited by T. Rowland Hill, M.D. Price, $5. Pp. 414, with 90 illustrations. Baltimore: William Wood & Company, 1939.

The title of this work, far from overstating the potential worth of the volume, really is but a modest indication of an excellent storehouse of facts, information and suggestions for the diagnosis, treatment and management of surgical and medical conditions in their many ramifications. A review of this book gives one the definite conviction that it is of unusual value and excellence. Each chapter, on a different subject and by a separate author, is a splendid presentation of facts in reference to a specific subject, coupled with an argosy of pertinent information gained through the author's all-absorbing interest in that subject. It would be difficult indeed to select any one chapter as more outstanding or of more interest or value than another. The subjects presented will appeal alike to specialists and general practitioners, and the volume will make a most valuable addition to the library of any one actively engaged in the practice of medicine. It is rare indeed that a book so all embracing in the subjects on which it touches is presented with such excellence and clarity and by such a galaxy of unusual writers, who have gleaned their thoughts and ideas from practice in their chosen fields.

Directory of Pediatric Societies*

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

American Committee:

Chairman: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
General Secretary: Dr. Kenneth D. Blackfan, 300 Longwood Ave., Boston.
Assistant Secretary-Treasurer: Dr. Charles F. McKhann, 300 Longwood Ave., Boston.

Canadian Committee:

Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Place: Boston, Mass. Time: Postponed indefinitely.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

British Paediatric Association

President: Prof. Charles McNeil, 44 Heriot Row, Edinburgh, Scotland.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

SOCIEDAD CUBANA DE PEDIATRÍA

President: Dr. Clemente Inclan Costa, Manrique 48, Habana.
Secretary: Dr. Serafin Falcon Lopez, Calle B No. 356, Vedado, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Jorge Muñoz Turnbull, Av. Alvaro Obregón 186, Mexico, D. F.
Secretary: Dr. Fernando López Clares, Medellín 191, Mexico, D. F.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue du Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Secretary: Dr. Hugh L. Dwyer, 315 Alameda Rd., Kansas City, Mo.
Place: New York. Time: June 10-14, 1940.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. J. B. Bilderback, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Hotel Peabody, Memphis, Tenn. Time: Nov. 18-20, 1940.
Region II. Place: Richmond, Va.
Region III. Place: Hotel Muehlbach, Kansas City, Mo. Time: May 16-18, 1940.
Region IV. Place: Seattle, Wash. Time: May 30-June 1, 1940.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S HOSPITAL SECTION

Chairman: Miss Mabel Binner, Children's Memorial Hospital, Chicago.
Secretary: Winifred Culbertson, Children's Convalescent Hospital, Cincinnati.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Herbert B. Wilcox, 39 E. 75th St., New York.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. L. M. Lindsay, 815 Medical Arts Bldg., Montreal.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

Society for Pediatric Research

President: Dr. Daniel C. Darrow, 330 Cedar St., New Haven, Conn.
Secretary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia.

SECTIONAL

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

President: Dr. R. Cannon Eley, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

North Pacific Pediatric Society

President: Dr. S. G. Henricke, 4215 N. E. Hancock St., Portland, Ore.
Secretary: Dr. J. S. Backstrand, 388 State St., Salem, Ore.

Rocky Mountain Pediatric Society

President: Dr. John Schoonover, Republic Bldg., Denver.
Secretary: Dr. F. Craig Johnson, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7:30 p. m.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.
Secretary: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables, Fla.

STATE

Alabama Pediatric Society

President: Dr. Stewart H. Welch, 1117 S. 20th St., Birmingham.
Secretary-Treasurer: Dr. William R. Britton, 4 Catoma St., Montgomery.

Arkansas State Pediatric Association

Chairman: Dr. G. D. Murphy, 112 Peach St., El Dorado.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.

California State Medical Society, Section on Pediatrics

Chairman: Dr. Harold K. Faber, 2341 Clay St., San Francisco.
Secretary: Dr. Hartzel H. Ray, 23–2d Ave., San Mateo.

Florida State Pediatric Society

President: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables.
Secretary: Dr. George N. Leonard, 605 Lincoln Rd., Miami Beach.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. L. H. Muse, 384 Peachtree St. N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. Oliver L. Stringfield, 1416 Bedford St., Stamford.
Secretary: Dr. Joseph L. Hetzel, 103 N. Main St., Waterbury.
Time: Three meetings a year.

Illinois State Medical Society, Section on Pediatrics

Chairman: Dr. H. William Elghammer, 5307 Hyde Park Blvd., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: Peoria. Time: May 22, 1940.

Indiana State Pediatric Society

President: Dr. O. N. Torian, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Morgan J. Foster, 837 Higley Bldg., Cedar Rapids.
Secretary-Treasurer: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.

Louisiana State Pediatric Society

President: Dr. H. Aubrey White, Alexandria.
Secretary-Treasurer: Dr. W. C. Rivenbark, 220 Physicians and Surgeons Bldg., New Orleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Paul W. Beaven, 26 S. Goodman St., Rochester.
Secretary: Dr. Leslie O. Ashton, 850 Park Ave., New York.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. John M. Higgins, 600 S. Wilbur Ave., Sayre.
Secretary: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Allan L. Richardson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. Ward L. Chadwick, 524 Medical Arts Bldg., Grand Rapids.

Mississippi State Pediatric Society

President: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Secretary-Treasurer: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Place: To be designated by society. Time: Yearly.

Nebraska Pediatric Society

President: Dr. Herman M. Jahr, 1120 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. Elmer W. Bantin, 440 Aquila Court Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. Marion Y. Keith, 369 N. Elm St., Greensboro.
Secretary: Dr. G. W. Kutscher Jr., 176 Woodfin St., Asheville.

Oklahoma State Pediatric Society

President: Dr. J. B. Snow, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Place: Oklahoma Club. Time: 6:30 p. m., fourth Friday of each alternate month from September to May, inclusive.

South Carolina Pediatric Society

President: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.
Secretary-Treasurer: Dr. William Weston Jr., 1428 Lady St., Columbia.

Tennessee State Pediatric Society

President: Dr. William E. Van Order, 546 McCallie Ave., Chattanooga.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.

Texas Pediatric Society

President: Dr. T. A. Tumbleson, 2100 North St., Beaumont.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Dallas. Time: May 15, 1940.

Virginia Pediatric Society

President: Dr. W. Ambrose McGee, 616 W. Grace St., Richmond.
Secretary: Dr. John M. Bishop, Medical Arts Bldg., Roanoke.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. J. L. Blanton, 207 Fairmont Ave., Fairmont.
Secretary: Dr. Theresa O. Snaith, 450 Center Ave., Weston.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. N. C. Wetzel, 2103 Adelbert Rd., Cleveland.
Secretary: Dr. Fred Rittenger, 10515 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto, Canada.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto, Canada.

Bronx Pediatric Society

President: Dr. Harry S. Altman, 940 Grand Concourse, New York.
Secretary: Dr. David Zahn, 2474 Valentine Ave., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Benjamin Kramer, 6 Pierrepont St., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank van der Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Tuesday of April and September.

Chicago Pediatric Society

President: Dr. Gerard N. Krost, 2376 E. 71st St., Chicago.
Secretary: Dr. George F. Munns, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

Dallas Pediatric Society

President: Dr. Edgar Loomis, 351 W. Jefferson Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. William O'Donnell, 1553 Woodward Ave., Detroit.
Secretary: Dr. Robert Mason, 5140–2d Blvd., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Stephen C. Redd, 157 Forrest Ave. N. E., Atlanta.
Secretary: Dr. C. Dixon Fowler, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Thomas J. Donovan, 3820 Fannin St., Houston, Texas.
Secretary: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. John Aull, 1103 Grand Ave., Kansas City.
Secretary: Dr. George Herrman, 1107 Bryant Bldg., Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. H. R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Paul M. Hamilton, 248 E. Main St., Alhambra, Calif.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Benjamin Stoloff, 1149 Eastern Parkway, Brooklyn.
Secretary: Dr. Harry Apfel, 988 Park Pl., Brooklyn, N. Y.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., second Monday of each month, October to March, inclusive.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. James Dobbins, 42-04 Ditmars Blvd., Long Island City, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144–38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. Harry H. Donnally, 1612 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. Harry A. Spigel, 2647 Connecticut Ave. N. W. Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., fourth Thursday of October, January, February, March and April.

Memphis Pediatric Society

President: Dr. Barton Etter, 376 S. Bellevue St., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. S. F. Morgan, 5630 N. Lake Dr., Milwaukee.
Secretary-Treasurer: Dr. F. R. Janney, 1411 Wauwatosa Ave., Wauwatosa, Wis.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Rustin McIntosh, Babies Hospital, New York.
Secretary: Dr. Leslie O. Ashton, 850 Park Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Roland E. Nutting, 205 W. 2d St., Duluth, Minn.
Secretary-Treasurer: Dr. John M. Adams, 1009 Nicollet Ave., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Oklahoma City Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Time: Every month, except June, July and August.

Philadelphia Pediatric Society

President: Dr. Pascal F. Lucchesi, 4000 N. Front St., Philadelphia.
Secretary: Dr. Aims C. McGuinness, Children's Hospital, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to April, inclusive.

Pittsburgh Pediatric Society

President: Dr. E. R. McClusky, 3200–5th Ave., Pittsburgh.
Secretary-Treasurer: Dr. Carl Ruder, 646 Washington Rd., Mount Lebanon, Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

Richmond Pediatric Society

President: Dr. Charles L. Outland, 312 N. 9th St., Richmond, Va.
Secretary-Treasurer: Dr. T. Stanley Meade, 913 Floyd Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

Rochester Pediatric Society

President: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Secretary: Dr. W. L.. Bradford, 16 N. Goodman St., Rochester, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee. Time: Second Friday of each month.

St. Louis Pediatric Society

President: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Secretary-Treasurer: Dr. Peter G. Danis, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society Bldg. Time: Third Friday of ech month from September to June.

Seattle Pediatric Society

President: Dr. Jay I. Durand, 1305–4th Ave., Seattle.
Secretary: Dr. Frederick B. Joy, 1215–4th Ave., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Norman Nixon, 1136 W. 6th St., Los Angeles.
Secretary: Dr. Donald C. Shelby, 3780 Wilshire Blvd., Los Angeles.
Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Yark Osterlin, Central Michigan Children's Clinic, Traverse City, Mich.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Time: Nov. 15-16, 1940.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. M. Bernard Brahdy, 531 E. Lincoln Ave., Mount Vernon.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Ave., Rye.
Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October. December, February and April.